
**Combination of epigenetic factors and bispecific compounds targeting CD33 and CD3
in the treatment of myeloid leukemia**

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Field of the Invention

The present invention provides a combination epigenetic factors and bispecific compounds targeting CD33 and CD3 in the treatment of myeloid leukemia, wherein the epigenetic factor is selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors, hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone demethylase inhibitors and ATRA (All Trans-retinoic acid). Accordingly, the invention provides a pharmaceutical composition comprising a CD33 targeting compound and at least one epigenetic factor and an epigenetic factor for use in the amelioration, and/or treatment of a myeloid leukemia, wherein the epigenetic factor increases the responsiveness of a patient to a CD33 targeting compound. Moreover, the invention provides the use of at least one an epigenetic factor for increasing the responsiveness of a myeloid leukemia patient to a treatment with a CD33 targeting compound, a method for the treatment of a myeloid leukemia, the method comprising the administration of at least one epigenetic factor and a CD33 targeting compound to a patient in the need thereof and a kit comprising a pharmaceutical composition of the invention or an epigenetic factor of the invention and a bispecific CD33 targeting compound.

Background of the invention

Despite some gradual improvements over the last decades with the use of intensive therapies – including multiagent conventional chemotherapy and allogeneic stem cell transplantation (SCT) – the survival of patients with acute myeloid leukemia (AML) remains poor, and patient are at high risk of experiencing treatment-related morbidity and mortality. For example, although SCT has proven to provide a potent anti-leukemic effect that can lead to elimination of chemoresistant leukemic cells, a large number of patients will develop significant graft versus host (GvH) disease that will eventually be fatal in many. For many patients, in particular those who are not suitable for such intensive therapeutic strategies, novel therapeutic options including immunotherapeutic approaches are urgently sought after. A promising immunotherapeutic strategy devoid of GvH reactions is to recruit in-vivo the patient's own T-cells and retarget them directly at leukemic cells.

This approach became feasible by a novel class of bispecific single-chain antibodies, which direct cytotoxic T-lymphocytes at predefined surface antigens on tumor cells (Baeuerle et al. Curr Opin Mol Ther. 2009;11:22-30). Clinical proof of concept was provided by

blinatumomab, a bispecific antibody directed at both the CD19 B-cell surface antigen and the CD3 ϵ component of the T-cell receptor complex. Its therapeutic efficacy was shown for patients with B-cell lymphomas and B precursor acute lymphoblastic leukemia (ALL).

Acute myeloid leukemia (AML) has served as paradigm for the therapeutic use of monoclonal antibodies because of well-defined cell surface antigens and easy tumor accessibility. The most investigated target so far is CD33, a sialic-acid-dependent cytoadhesion molecule known as a myeloid differentiation antigen found on AML blasts in most patients and, perhaps, leukemic stem cells in some. While the intact humanized CD33 antibody lintuzumab induced complete remission in individual patients in a single-agent phase I and II trial, no survival benefit was found in a phase III trial when it was combined with a triple chemotherapy regimen.

Summary of the invention

The present invention provides a pharmaceutical composition comprising a CD33 targeting compound and at least one epigenetic factor, wherein

- (a) the CD33 targeting compound is a bispecific construct comprising a first binding domain specifically binding to CD33 and a second binding domain specifically binding to CD3; and
- (b) the at least one epigenetic factor is selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors, hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone methyltransferase (HMT) inhibitors and ATRA (All Trans-retinoic acid).

In one embodiment the pharmaceutical composition of the invention is characterized in a way that the at least one epigenetic factor is selected from the group comprising:

- (a) a histone deacetylase (HDAC) inhibitor selected from the group consisting of panobinostat, vorinostat, romidepsin, N-acetyldinaline, belinostat, givinostat, entinostat, mocetinostat, EVP-0334, SRT501, CUDC-101, Quisinostat, abexinostat, LAQ824, and valproic acid;
- (b) a DNA methyltransferase (DNMT) I inhibitor selected from the group consisting of 5-azacitidine, decitabine, hydralazine, zebularine, procainamide, (-)-epigallocatechin-3-gallate, MG98, RG108, and SGI-110; and
- (c) a histone methyltransferase (HMT) inhibitor selected from the group consisting of LSD1 (KDM1A) demethylase inhibitor, and chaetocin.

The invention also provides a pharmaceutical composition, wherein

- (a) the epigenetic factor is administered prior to the administration of the CD33 targeting compound;

- (b) the epigenetic factor is administered subsequent to the administration of the CD33 targeting compound; or
- (c) the epigenetic factor and the CD33 targeting compound are administered simultaneously.

5 The invention further provides a pharmaceutical composition, wherein a first dose of the epigenetic factor is administered prior to the start of the administration of the CD33 targeting compound.

Moreover, the invention further provides a pharmaceutical composition, wherein the administration of the epigenetic factor is continued during the administration of the CD33 targeting compound.

In one embodiment the pharmaceutical composition of the invention is characterized in a way that the bispecific construct is a bispecific antibody construct.

In preferred embodiment of the pharmaceutical composition of the invention the bispecific antibody construct is a bispecific single chain antibody construct.

15 It is also preferred for the pharmaceutical composition of the invention that the bispecific antibody construct binds to human and cynomolgous CD3 and human and cynomolgous CD33.

In one embodiment of the pharmaceutical composition of invention the bispecific antibody construct comprises

- 20 • a first binding domain specifically binding to CD33 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 6, 24, 42, 60, 78, 96, 114 and 132 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 1, 19, 37, 55, 73, 91, 109 and 127; and
- a second binding domain specifically binding to CD3 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 154, 157, 160, 163, 166, 169 and 172 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 155, 158, 161, 164, 167, 170 and 173.

In preferred embodiment of the pharmaceutical composition the bispecific antibody construct comprises an amino acid sequence as depicted in any of SEQ ID NOs: 13, 15, 17, 31, 33, 35, 49, 51, 53, 67, 69, 71, 85, 87, 89, 103, 105, 107, 121, 123, 125, 139, 141, 143, 148, 150, 152, 215, 217, 219, 221, 223, 225 and 227.

The pharmaceutical composition of the invention is envisaged for the treatment of CD33 expressing myeloid leukemia. Preferably, the myeloid leukemia is selected from the group consisting of acute myeloblastic leukemia, chronic neutrophilic leukemia, myeloid dendritic cell leukemia, accelerated phase chronic myelogenous leukemia, acute myelomonocytic leukemia, juvenile myelomonocytic leukemia, chronic myelomonocytic leukemia, acute basophilic leukemia, acute eosinophilic leukemia, chronic eosinophilic leukemia, Acute

megakaryoblastic leukemia, essential thrombocytosis, acute erythroid leukemia, polycythemia vera, myelodysplastic syndrome, acute panmyelosis, myeloid sarcoma, and acute biphenotypic leukaemia.

In an alternative embodiment the invention provides an epigenetic factor for use in the amelioration and/or treatment of a myeloid leukemia, wherein the epigenetic factor increases the responsiveness of a patient to a CD33 targeting compound, wherein

(a) the CD33 targeting compound is a bispecific construct comprising a first binding domain specifically binding to CD33 and a second binding domain specifically binding to CD3; and

(b) the at least one epigenetic factor is selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors, hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone methyltransferase (HMT) inhibitors and ATRA (All Trans-retinoic acid).

In one embodiment of the epigenetic factor of the invention the epigenetic factor is selected from the group comprising

(a) a histone deacetylase (HDAC) inhibitor selected from the group consisting of panobinostat, vorinostat, romidepsin, N-acetyldinaline, belinostat, givinostat, entinostat, mocetinostat, EVP-0334, SRT501, CUDC-101, Quisinostat, abexinostat, LAQ824, and valproic acid;

(b) a DNA methyltransferase (DNMT) I inhibitor selected from the group consisting of 5-azacitidine, decitabine, hydralazine, zebularine, procainamide, (-)-epigallocatechin-3-gallate, MG98, RG108, and SGI-110; and

(c) a histone methyltransferase (HMT) inhibitor selected from the group consisting of LSD1 (KDM1A) demethylase inhibitor, and chaetocin.

Moreover, in one embodiment of the epigenetic factor of the invention

(a) the epigenetic factor is administered prior to the administration of the CD33 targeting compound;

(b) the epigenetic factor is administered subsequent to the administration of the CD33 targeting compound; or

(c) the epigenetic factor and the CD33 targeting compound are administered simultaneously.

It is preferred for the epigenetic factor of the invention that a first dose of the epigenetic factor is administered prior to the start of the administration of the CD33 targeting compound.

Preferably, the administration of the epigenetic factor of the invention is continued during the administration of the CD33 targeting compound.

It is also preferred for the epigenetic factor the invention that the bispecific construct is a bispecific antibody construct.

In one embodiment of the epigenetic factor of the invention the bispecific antibody construct is a bispecific single chain antibody construct.

- 5 It is preferred for the epigenetic factor of the invention that the bispecific antibody construct binds to human and cynomolgous CD3 and CD33.

Also preferred for the epigenetic factor of the invention is that the bispecific antibody construct comprises

- a first binding domain specifically binding to CD33 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 6, 24, 42, 60, 78, 96, 114 and 132 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 1, 19, 37, 55, 73, 91, 109 and 127; and
- a second binding domain specifically binding to CD3 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 154, 157, 160, 163, 166, 169 and 172 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 155, 158, 161, 164, 167, 170 and 173.

In one embodiment of the epigenetic factor of the invention the bispecific antibody construct comprises an amino acid sequence as depicted in any of SEQ ID NOs: 13, 15, 17, 31, 33, 35, 49, 51, 53, 67, 69, 71, 85, 87, 89, 103, 105, 107, 121, 123, 125, 139, 141, 143, 148, 150, 152, 215, 217, 219, 221, 223, 225 and 227.

In one embodiment of the epigenetic factor of the invention the myeloid leukemia is selected from the group consisting of acute myeloblastic leukemia, chronic neutrophilic leukemia, myeloid dendritic cell leukemia, accelerated phase chronic myelogenous leukemia, acute myelomonocytic leukemia, juvenile myelomonocytic leukemia, chronic myelomonocytic leukemia, acute basophilic leukemia, acute eosinophilic leukemia, chronic eosinophilic leukemia, Acute megakaryoblastic leukemia, essential thrombocytosis, acute erythroid leukemia, polycythemia vera, myelodysplastic syndrome, acute panmyelosis, myeloid sarcoma, and acute biphenotypic leukaemia.

An alternative embodiment of the invention provides a use of at least one an epigenetic factor for increasing the responsiveness of a myeloid leukemia patient to a treatment with a CD33 targeting compound, wherein

- (a) the CD33 targeting compound is a bispecific construct comprising a first binding domain specifically binding to CD33 and a second binding domain specifically binding to CD3; and
- (b) the at least one epigenetic factor is selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors,

hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone demethylase inhibitors and ATRA (All Trans-retinoic acid).

In one embodiment of the use of the invention the at least one epigenetic factor is selected from the group comprising

- 5 (a) a histone deacetylase (HDAC) inhibitor selected from the group consisting of panobinostat, vorinostat, romidepsin, N-acetyldinaline, belinostat, givinostat, entinostat, mocetinostat, EVP-0334, SRT501, CUDC-101, Quisinostat, abexinostat, LAQ824, and valproic acid;
- 10 (b) a DNA methyltransferase (DNMT) I inhibitor selected from the group consisting of 5-azacitidine, decitabine, hydralazine, zebularine, procainamide, (-)-epigallocatechin-3-gallate, MG98, RG108, and SGI-110; and
- (c) a histone methyltransferase (HMT) inhibitor selected from the group consisting of LSD1 (KDM1A) demethylase inhibitor, and chaetocin.

Also in an embodiment of the use of the invention

- 15 (a) the epigenetic factor is administered prior to the administration of the CD33 targeting compound;
- (b) the epigenetic factor is administered subsequent to the administration of the CD33 targeting compound; or
- 20 (c) the epigenetic factor and the CD33 targeting compound are administered simultaneously.

In a preferred use of any of the invention a first dose of the epigenetic factor is administered prior to the start of the administration of the CD33 targeting compound.

Moreover, in one embodiment of the use of the invention the administration of the epigenetic factor is continued during the administration of the CD33 targeting compound.

- 25 In one embodiment of the use of the invention the bispecific construct is a bispecific antibody construct.

In a preferred embodiment of the use of the invention the bispecific antibody construct is a bispecific single chain antibody construct.

- 30 In one embodiment of the use of the invention the bispecific antibody construct binds to human and cynomolgous CD3 and CD33.

According to one embodiment of the use of the invention the bispecific antibody construct comprises

- a first binding domain specifically binding to CD33 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 6, 24, 42, 60, 78, 96, 114 and 132 and a
- 35 VH chain having an amino acid sequence as depicted in SEQ ID NO: 1, 19, 37, 55, 73, 91, 109 and 127; and

- a second binding domain specifically binding to CD3 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 154, 157, 160, 163, 166, 169 and 172 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 155, 158, 161, 164, 167, 170 and 173.

5 In a preferred embodiment of the use of the invention the bispecific antibody construct comprises an amino acid sequence as depicted in any of SEQ ID NOs: 13, 15, 17, 31, 33, 35, 49, 51, 53, 67, 69, 71, 85, 87, 89, 103, 105, 107, 121, 123, 125, 139, 141, 143, 148, 150, 152, 215, 217, 219, 221, 223, 225 and 227.

Furthermore, in an embodiment of the use of the invention the myeloid leukemia is selected
 10 from the group consisting of acute myeloblastic leukemia, chronic neutrophilic leukemia, myeloid dendritic cell leukemia, accelerated phase chronic myelogenous leukemia, acute myelomonocytic leukemia, juvenile myelomonocytic leukemia, chronic myelomonocytic leukemia, acute basophilic leukemia, acute eosinophilic leukemia, chronic eosinophilic leukemia, Acute megakaryoblastic leukemia, essential thrombocytosis, acute erythroid
 15 leukemia, polycythemia vera, myelodysplastic syndrome, acute panmyelosis, myeloid sarcoma, and acute biphenotypic leukaemia.

In a further alternative embodiment the invention provides a method for the treatment of a myeloid leukemia, the method comprising the administration of at least one epigenetic factor and a CD33 targeting compound to a patient in the need thereof, wherein

- 20 (a) the CD33 targeting compound is a bispecific construct comprising a first binding domain specifically binding to CD33 and a second binding domain specifically binding to CD3; and
- (b) the at least one epigenetic factor is selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors,
 25 hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone methyltransferase (HMT) inhibitors and ATRA (All Trans-retinoic acid).

In an embodiment of the method of the invention the at least one epigenetic factor is selected from the group comprising

- 30 (a) a histone deacetylase (HDAC) inhibitor selected from the group consisting of panobinostat, vorinostat, romidepsin, N-acetyldinaline, belinostat, givinostat, entinostat, mocetinostat, EVP-0334, SRT501, CUDC-101, Quisinostat, abexinostat, LAQ824, and valproic acid;
- (b) a DNA methyltransferase (DNMT) I inhibitor selected from the group consisting of 5-azacitidine, decitabine, hydralazine, zebularine, procainamide, (-)-epigallocatechin-3-gallate, MG98, RG108, and SGI-110; and
 35 (c) a histone methyltransferase (HMT) inhibitor selected from the group consisting of LSD1 (KDM1A) demethylase inhibitor, and chaetocin.

Also in an embodiment of the method of the invention

- (a) the epigenetic factor is administered prior to the administration of the CD33 targeting compound;
- (b) the epigenetic factor is administered subsequent to the administration of the CD33 targeting compound; or
- (c) the epigenetic factor and the CD33 targeting compound are administered simultaneously.

In a preferred embodiment of the method of the invention a first dose of the epigenetic factor is administered prior to the start of the administration of the CD33 targeting compound.

It is also preferred for the method of the invention that the administration of the epigenetic factor is continued during the administration of the CD33 targeting compound.

In one embodiment of the method of the invention the bispecific construct is a bispecific antibody construct.

It is preferred for the method of the invention that the bispecific antibody construct is a bispecific single chain antibody construct.

It is more preferred for the method of the invention that the bispecific antibody construct binds to human and cynomolgous CD3 and CD33.

In one embodiment of the method of the invention the bispecific antibody construct comprises

- a first binding domain specifically binding to CD33 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 6, 24, 42, 60, 78, 96, 114 and 132 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 1, 19, 37, 55, 73, 91, 109 and 127; and
- a second binding domain specifically binding to CD3 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 154, 157, 160, 163, 166, 169 and 172 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 155, 158, 161, 164, 167, 170 and 173.

Also in one embodiment of the method of the invention the bispecific antibody construct comprises an amino acid sequence as depicted in any of SEQ ID NOs: 13, 15, 17, 31, 33, 35, 49, 51, 53, 67, 69, 71, 85, 87, 89, 103, 105, 107, 121, 123, 125, 139, 141, 143, 148, 150, 152, 215, 217, 219, 221, 223, 225 and 227.

Furthermore, in one embodiment of the method of the invention the myeloid leukemia is selected from the group consisting of acute myeloblastic leukemia, chronic neutrophilic leukemia, myeloid dendritic cell leukemia, accelerated phase chronic myelogenous leukemia, acute myelomonocytic leukemia, juvenile myelomonocytic leukemia, chronic myelomonocytic leukemia, acute basophilic leukemia, acute eosinophilic leukemia, chronic eosinophilic leukemia, Acute megakaryoblastic leukemia, essential thrombocytosis, acute

erythroid leukemia, polycythemia vera, myelodysplastic syndrome, acute panmyelosis, myeloid sarcoma, and acute biphenotypic leukaemia.

A further alternative embodiment of the invention provides a kit comprising a pharmaceutical composition of the invention or an epigenetic factor of the invention and a bispecific CD33 targeting compound comprising a first binding domain specifically binding to CD33 and a second binding domain specifically binding to CD3, to be employed in the amelioration and/or treatment of a myeloid leukemia.

Brief description of the drawings

Figure 1:

Effect of panobinostat pretreatment on CD33 expression and AMG 330-induced cytotoxicity. Parental OCI-AML3 and KG-1a cells were either left untreated or pretreated with panobinostat for 72 hours. Subsequently, CD33 expression was quantified, and cells treated with/without AMG 330 (0-250 pg/mL) and various effector:target (E:T) cell ratios using healthy donor T-cells. 48 hours later, cell counts were determined and cytotoxicity was assessed with DAPI staining to quantify drug-specific cytotoxicity. Results are shown as mean±SEM from 3 independent experiments performed in duplicate wells using a single healthy donor as source for exogenous T-cells.

Figure 2:

Effect of azacitidine pretreatment on CD33 expression and AMG 330-induced cytotoxicity. Parental KG-1a cells were either left untreated or pretreated with azacitidine for 72 hours. Subsequently, CD33 expression was quantified, and cells treated with/without AMG 330 (0-250 pg/mL) and various effector:target (E:T) cell ratios using healthy donor T-cells. 48 hours later, cell counts were determined and cytotoxicity was assessed with DAPI staining to quantify drug-specific cytotoxicity. Results are shown as mean±SEM from 3 independent experiments performed in duplicate wells using a single healthy donor as source for exogenous T-cells.

Figure 3:

Hydroxyurea-concentration dependant up-regulation of CD33 on A) HL-60 and B) PL21 AML cells.

Figure 4:

Hydroxyurea dependant up-regulation of CD33 on primary AML cells from patient 2.

Figure 5:

G-CSF dependant up-regulation of CD33 on KG1α AML cells after 10 days of incubation.

Figure 6:

G-CSF dependant up-regulation of CD33 on primary AML cells from patient 1 after 10 days of incubation.

Detailed description of the invention

Definitions:

It must be noted that as used herein, the singular forms "a", "an", and "the", include plural references unless the context clearly indicates otherwise. Thus, for example, reference to "a reagent" includes one or more of such different reagents and reference to "the method" includes reference to equivalent steps and methods known to those of ordinary skill in the art that could be modified or substituted for the methods described herein.

Unless otherwise indicated, the term "at least" preceding a series of elements is to be understood to refer to every element in the series. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the present invention.

The term "and/or" wherever used herein includes the meaning of "and", "or" and "all or any other combination of the elements connected by said term".

The term "about" or "approximately" as used herein means within $\pm 20\%$, preferably within $\pm 15\%$, more preferably within $\pm 10\%$, and most preferably within $\pm 5\%$ of a given value or range.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integer or step. When used herein the term "comprising" can be substituted with the term "containing" or "including" or sometimes when used herein with the term "having".

When used herein "consisting of" excludes any element, step, or ingredient not specified in the claim element. When used herein, "consisting essentially of" does not exclude materials or steps that do not materially affect the basic and novel characteristics of the claim.

In each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms.

The term "CD33 targeting compound" defines in the context of the present invention a binding molecule capable of specifically binding to the extracellular domain of the cell surface molecule CD33. As mentioned above CD33, a sialic-acid-dependent cytoadhesion molecule, is known as a myeloid differentiation antigen found on AML blasts in most patients. As apparent from the description of the embodiments of the invention, the CD33

targeting compound in the sense of the invention is a bispecific compound comprising at least a binding domain for the extracellular domain of the cell surface molecule CD33 and the extracellular domain of the molecule CD3 expressed on T cells. It is emphasized that the CD33 targeting compound comprises in the sense of the invention at least the binding domain for CD33 and CD3 and may also comprise one or more additional binding domains for other target structures, which result in a tri- or multispecific compound. In other words, the term "CD33 targeting compound" in the sense of the present disclosure indicates any molecule capable of (specifically) binding to, interacting with or recognizing the target molecule CD33 on the surface of a target cell and CD3 on the surface of a T cell. Such molecules or constructs may include proteinaceous parts and non-proteinaceous parts (e.g. chemical linkers or chemical cross-linking agents such as glutaraldehyde).

The term "binding molecule" in the sense of the present disclosure indicates any molecule capable of (specifically) binding to, interacting with or recognizing the target molecule.

A binding molecule, so to say, provides the scaffold for said one or more binding domains so that said binding domains can bind/interact with the surface molecule on a target cell and CD3 receptor complex on a T cell. For example, such a scaffold could be provided by protein A, in particular, the Z-domain thereof (affibodies), ImmE7 (immunity proteins), BPTI/APPI (Kunitz domains), Ras-binding protein AF-6 (PDZ-domains), charybdotoxin (Scorpion toxin), CTLA-4, Min-23 (knottins), lipocalins (anticalins), neokarzinostatin, a fibronectin domain, an ankyrin consensus repeat domain (Stumpp et al., Curr Opin Drug Discov Devel. 10(2), 153-159 (2007)) or thioredoxin (Skerra, Curr. Opin. Biotechnol. 18, 295-304 (2005); Hosse et al., Protein Sci. 15, 14-27 (2006); Nicaise et al., Protein Sci. 13, 1882-1891 (2004); Nygren and Uhlen, Curr. Opin. Struc. Biol. 7, 463-469 (1997)). A preferred binding molecule is an antibody, more preferably a bispecific antibody.

The term "single chain binding molecule" defines in connection with the present invention that the disclosed binding molecules in its simplest form are monomers. The molecules or constructs may include proteinaceous parts and non-proteinaceous parts (e.g. chemical linkers or chemical cross-linking agents such as glutaraldehyde). Thus, the single chain binding molecule may comprising accordance with the invention non-peptide linkers preferably to link at least two of the binding domains. Also in line with this invention are herein defined peptide linkers.

The definition of the term "antibody" includes embodiments such as monoclonal, chimeric, single chain, humanized and human antibodies, as well as antibody fragments, like, inter alia, Fab fragments. Antibody fragments or derivatives further comprise F(ab')₂, Fv, scFv fragments or single domain antibodies such as domain antibodies or nanobodies, single

variable domain antibodies or immunoglobulin single variable domain comprising merely one variable domain, which might be VHH, VH or VL, that specifically bind an antigen or epitope independently of other V regions or domains; see, for example, Harlow and Lane (1988) and (1999), loc. cit.; Kontermann and Dübel, Antibody Engineering, Springer, 2nd ed. 2010 and
5 Little, Recombinant Antibodies for Immunotherapy, Cambridge University Press 2009. Such immunoglobulin single variable domain encompasses not only an isolated antibody single variable domain polypeptide, but also larger polypeptides that comprise one or more monomers of an antibody single variable domain polypeptide sequence.

Monovalent antibody fragments in line with the above definition describe an embodiment of a
10 binding domain in connection with this invention. Such monovalent antibody fragments bind to a specific antigen and can be also designated "antigen-binding domain", "antigen-binding fragment" or "antibody binding region".

In line with this definition all above described embodiments of the term antibody can be subsumed under the term "antibody construct". Said term also includes diabodies or Dual-
15 Affinity Re-Targeting (DART) antibodies. Further envisaged are (bispecific) single chain diabodies, tandem diabodies (Tandab's), „minibodies“ exemplified by a structure which is as follows: (VH-VL-CH3)₂, (scFv-CH3)₂ or (scFv-CH3-scFv)₂, „Fc DART“ antibodies and „IgG DART“ antibodies, and multibodies such as triabodies. Immunoglobulin single variable domains encompass not only an isolated antibody single variable domain polypeptide, but
20 also larger polypeptides that comprise one or more monomers of an antibody single variable domain polypeptide sequence.

Various procedures are known in the art and may be used for the production of such antibody constructs (antibodies and/or fragments). Thus, (antibody) derivatives can be produced by peptidomimetics. Further, techniques described for the production of single
25 chain antibodies (see, inter alia, US Patent 4,946,778, Kontermann and Dübel (2010), loc. cit. and Little(2009), loc. cit.) can be adapted to produce single chain antibodies specific for elected polypeptide(s). Also, transgenic animals may be used to express humanized antibodies specific for polypeptides and fusion proteins of this invention. For the preparation of monoclonal antibodies, any technique, providing antibodies produced by continuous cell
30 line cultures can be used. Examples for such techniques include the hybridoma technique (Köhler and Milstein Nature 256 (1975), 495-497), the trioma technique, the human B-cell hybridoma technique (Kozbor, Immunology Today 4 (1983), 72) and the EBV-hybridoma technique to produce human monoclonal antibodies (Cole et al., Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, Inc. (1985), 77-96). Surface plasmon resonance as employed
35 in the BIAcore system can be used to increase the efficiency of phage antibodies which bind to an epitope of a target polypeptide, such as CD3 epsilon (Schier, Human Antibodies

Hybridomas 7 (1996), 97-105; Malmborg, J. Immunol. Methods 183 (1995), 7-13). It is also envisaged in the context of this invention that the term "antibody" comprises antibody constructs, which may be expressed in a host as described herein below, e.g. antibody constructs which may be transfected and/or transduced via, inter alia, viruses or plasmid vectors.

Furthermore, the term "antibody" as employed herein also relates to derivatives or variants of the antibodies described herein which display the same specificity as the described antibodies. Examples of "antibody variants" include humanized variants of non-human antibodies, "affinity matured" antibodies (see, e.g. Hawkins et al. J. Mol. Biol. 254, 889-896 (1992) and Lowman et al., Biochemistry 30, 10832- 10837 (1991)) and antibody mutants with altered effector function(s) (see, e.g., US Patent 5, 648, 260, Kontermann and Dübel (2010), loc. cit. and Little(2009), loc. cit.).

The terms "antigen-binding domain", "antigen-binding fragment" and "antibody binding region" when used herein refer to a part of an antibody molecule that comprises amino acids responsible for the specific binding between antibody and antigen. The part of the antigen that is specifically recognized and bound by the antibody is referred to as the "epitope" as described herein above. As mentioned above, an antigen-binding domain may typically comprise an antibody light chain variable region (VL) and an antibody heavy chain variable region (VH); however, it does not have to comprise both. Fd fragments, for example, have two VH regions and often retain some antigen-binding function of the intact antigen-binding domain. Examples of antigen-binding fragments of an antibody include (1) a Fab fragment, a monovalent fragment having the VL, VH, CL and CH1 domains; (2) a F(ab')₂ fragment, a bivalent fragment having two Fab fragments linked by a disulfide bridge at the hinge region; (3) a Fd fragment having the two VH and CH1 domains; (4) a Fv fragment having the VL and VH domains of a single arm of an antibody, (5) a dAb fragment (Ward et al., (1989) Nature 341 :544-546), which has a VH domain; (6) an isolated complementarity determining region (CDR), and (7) a single chain Fv (scFv). Although the two domains of the Fv fragment, VL and VH are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the VL and VH regions pair to form monovalent molecules (known as single chain Fv (scFv); see e.g., Huston et al. (1988) Proc. Natl. Acad. Sci USA 85:5879-5883). These antibody fragments are obtained using conventional techniques known to those with skill in the art, and the fragments are evaluated for function in the same manner as are intact antibodies.

In the event that a (synthetic) linker is used, this linker is preferably of a length and sequence sufficient to ensure that each of the first and second domains can, independently from one another, retain their differential binding specificities. Most preferably and as documented in

the appended examples, the antibody construct of the invention is a “bispecific single chain antibody construct”, more preferably a bispecific single chain Fv (scFv). Bispecific single chain molecules are known in the art and are described in WO 99/54440, Mack, J. Immunol. (1997), 158, 3965-3970, Mack, PNAS, (1995), 92, 7021-7025, Kufer, Cancer Immunol. Immunother., (1997), 45, 193-197, Löffler, Blood, (2000), 95, 6, 2098-2103, Brühl, Immunol., (2001), 166, 2420-2426, Kipriyanov, J. Mol. Biol., (1999), 293, 41-56. One example of a CD33 targeting compound in connection with the present invention, which is a bispecific single chain molecule is AMG330, which has also been used in the appended examples.

The said variable domains comprised in the herein described antibody constructs may be connected by additional linker sequences. The term “peptide linker” defines in accordance with the present invention an amino acid sequence by which the amino acid sequences of the first domain and the second domain of the antibody construct of the invention are linked with each other. An essential technical feature of such peptide linker is that said peptide linker does not comprise any polymerization activity. Preferred amino acid residues for a peptide linker include Gly, Ser and Thr are characterized by a length between 5 and 25 amino acid residues. Among the suitable peptide linkers are those described in U.S. Patents 4,751,180 and 4,935,233 or WO 88/09344. A preferred embodiment of a peptide linker is characterized by the amino acid sequence Gly-Gly-Gly-Gly-Ser, i.e. Gly₄Ser, or polymers thereof, i.e. (Gly₄Ser)_x, where x is an integer 1 or greater. The characteristics of said peptide linker, which comprise the absence of the promotion of secondary structures are known in the art and described e.g. in Dall’Acqua et al. (Biochem. (1998) 37, 9266-9273), Cheadle et al. (Mol Immunol (1992) 29, 21-30) and Raag and Whitlow (FASEB (1995) 9(1), 73-80). Peptide linkers which also do not promote any secondary structures are preferred. The linkage of said domains to each other can be provided by, e.g. genetic engineering, as described in the examples. Methods for preparing fused and operatively linked bispecific single chain constructs and expressing them in mammalian cells or bacteria are well-known in the art (e.g. WO 99/54440 or Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 2001).

For peptide linkers, which connect the at least two binding domains in the antibody construct of the invention peptide linkers are preferred which comprise only a few number of amino acid residues, e.g. 12 amino acid residues or less. Thus, peptide linker of 12, 11, 10, 9, 8, 7, 6 or 5 amino acid residues are preferred. An envisaged peptide linker with less than 5 amino acids comprises 4, 3, 2 or one amino acid(s) wherein Gly-rich linkers are preferred. A particularly preferred “single” amino acid in context of said “peptide linker” is Gly. Accordingly, said peptide linker may consist of the single amino acid Gly.

The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally occurring mutations and/or post- translation modifications (e.g., isomerizations, amidations) that may be present in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. Furthermore, in contrast to conventional (polyclonal) antibody preparations which typically include different antibodies directed against different determinants (epitopes), each monoclonal antibody is directed against a single determinant on the antigen. In addition to their specificity, the monoclonal antibodies are advantageous in that they are synthesized by the hybridoma culture, uncontaminated by other immunoglobulins. The modifier "monoclonal" indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies, and is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies to be used in accordance with the present invention may be made by the hybridoma method first described by Kohler *et al.*, Nature, 256: 495 (1975), or may be made by recombinant DNA methods (see, e.g., U. S. Patent No. 4,816,567). The "monoclonal antibodies" may also be isolated from phage antibody libraries using the techniques described in Clackson *et al.*, Nature, 352: 624-628 (1991) and Marks *et al.*, J. Mol. Biol., 222: 581-597 (1991), for example.

The term "human antibody" includes antibodies having variable and constant regions corresponding substantially to human germline immunoglobulin sequences known in the art, including, for example, those described by Kabat *et al.* (See Kabat *et al.* (1991) loc. cit.). The human antibodies of the invention may include amino acid residues not encoded by human germline immunoglobulin sequences (e.g., mutations introduced by random or site-specific mutagenesis in vitro or by somatic mutation in vivo), for example in the CDRs, and in particular, CDR3. The human antibody can have at least one, two, three, four, five, or more positions replaced with an amino acid residue that is not encoded by the human germline immunoglobulin sequence. It is emphasized that the definition of human antibodies as used herein also contemplates fully human antibodies, which include only non-artificially and/or genetically altered human sequences of antibodies as those can be derived by using technologies using systems such as the Xenomice.

Examples of "antibody variants" include humanized variants of non- human antibodies, "affinity matured" antibodies (see, e.g. Hawkins *et al.* J. Mol. Biol. 254, 889-896 (1992) and Lowman *et al.*, Biochemistry 30, 10832- 10837 (1991)) and antibody mutants with altered effector function (s) (see, e.g., US Patent 5, 648, 260, Kontermann and Dübel (2010), loc. cit. and Little(2009), loc. cit.).

As used herein, "in vitro generated antibody" refers to an antibody where all or part of the variable region (e.g., at least one CDR) is generated in a non-immune cell selection (e.g., an in vitro phage display, protein chip or any other method in which candidate sequences can be tested for their ability to bind to an antigen). This term thus preferably excludes sequences generated by genomic rearrangement in an immune cell.

The pairing of a VH and VL together forms a single antigen-binding site. The CH domain most proximal to VH is designated as CH1. Each L chain is linked to an H chain by one covalent disulfide bond, while the two H chains are linked to each other by one or more disulfide bonds depending on the H chain isotype. The VH and VL domains consist of four regions of relatively conserved sequences called framework regions (FR1, FR2, FR3, and FR4), which form a scaffold for three regions of hypervariable sequences (complementarity determining regions, CDRs). The CDRs contain most of the residues responsible for specific interactions of the antibody with the antigen. CDRs are referred to as CDR 1, CDR2, and CDR3. Accordingly, CDR constituents on the heavy chain are referred to as H1, H2, and H3, while CDR constituents on the light chain are referred to as L1, L2, and L3.

The term "variable" refers to the portions of the immunoglobulin domains that exhibit variability in their sequence and that are involved in determining the specificity and binding affinity of a particular antibody (i.e., the "variable domain(s)"). Variability is not evenly distributed throughout the variable domains of antibodies; it is concentrated in sub-domains of each of the heavy and light chain variable regions. These sub-domains are called "hypervariable" regions or "complementarity determining regions" (CDRs). The more conserved (i.e., non-hypervariable) portions of the variable domains are called the "framework" regions (FRM). The variable domains of naturally occurring heavy and light chains each comprise four FRM regions, largely adopting a β -sheet configuration, connected by three hypervariable regions, which form loops connecting, and in some cases forming part of, the β -sheet structure. The hypervariable regions in each chain are held together in close proximity by the FRM and, with the hypervariable regions from the other chain, contribute to the formation of the antigen-binding site (see Kabat *et al.*, loc. cit.). The constant domains are not directly involved in antigen binding, but exhibit various effector functions, such as, for example, antibody-dependent, cell-mediated cytotoxicity and complement activation.

The terms "CDR", and its plural "CDRs", refer to a complementarity determining region (CDR) of which three make up the binding character of a light chain variable region (CDRL1, CDRL2 and CDRL3) and three make up the binding character of a heavy chain variable region (CDRH1, CDRH2 and CDRH3). CDRs contribute to the functional activity of an antibody molecule and are separated by amino acid sequences that comprise scaffolding or

framework regions. The exact definitional CDR boundaries and lengths are subject to different classification and numbering systems. CDRs may therefore be referred to by Kabat, Chothia, contact or any other boundary definitions, including the numbering system described herein. Despite differing boundaries, each of these systems has some degree of overlap in what constitutes the so called "hypervariable regions" within the variable sequences. CDR definitions according to these systems may therefore differ in length and boundary areas with respect to the adjacent framework region. See for example Kabat, Chothia, and/or MacCallum (Kabat *et al.*, loc. cit.; Chothia *et al.*, J. Mol. Biol, 1987, 196: 901; and MacCallum *et al.*, J. Mol. Biol, 1996, 262: 732). However, the numbering in accordance with the so-called Kabat system is preferred. The CDR3 of the light chain and, particularly, CDR3 of the heavy chain may constitute the most important determinants in antigen binding within the light and heavy chain variable regions. In some antibody constructs, the heavy chain CDR3 appears to constitute the major area of contact between the antigen and the antibody. In vitro selection schemes in which CDR3 alone is varied can be used to vary the binding properties of an antibody or determine which residues contribute to the binding of an antigen.

"Consisting essentially of" means that the amino acid sequence can vary by about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15% relative to the recited SEQ ID NO: sequence and still retain biological activity, as described herein.

In some embodiments, the binding molecules described herein are isolated proteins or substantially pure proteins. An "isolated" protein is unaccompanied by at least some of the material with which it is normally associated in its natural state, for example constituting at least about 5%, or at least about 50% by weight of the total protein in a given sample. It is understood that the isolated protein may constitute from 5 to 99.9% by weight of the total protein content depending on the circumstances. For example, the protein may be made at a significantly higher concentration through the use of an inducible promoter or high expression promoter, such that the protein is made at increased concentration levels. The definition includes the production of an antigen binding protein in a wide variety of organisms and/or host cells that are known in the art.

For amino acid sequences, sequence identity and/or similarity is determined by using standard techniques known in the art, including, but not limited to, the local sequence identity algorithm of Smith and Waterman, 1981, *Adv. Appl. Math.* 2:482, the sequence identity alignment algorithm of Needleman and Wunsch, 1970, *J. Mol. Biol.* 48:443, the search for similarity method of Pearson and Lipman, 1988, *Proc. Nat. Acad. Sci. U.S.A.* 85:2444, computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575

Science Drive, Madison, Wis.), the Best Fit sequence program described by Devereux *et al.*, 1984, *Nucl. Acid Res.* 12:387-395, preferably using the default settings, or by inspection. Preferably, percent identity is calculated by FastDB based upon the following parameters: mismatch penalty of 1; gap penalty of 1; gap size penalty of 0.33; and joining penalty of 30,
5 "Current Methods in Sequence Comparison and Analysis," Macromolecule Sequencing and Synthesis, Selected Methods and Applications, pp 127-149 (1988), Alan R. Liss, Inc.

An example of a useful algorithm is PILEUP. PILEUP creates a multiple sequence alignment from a group of related sequences using progressive, pairwise alignments. It can also plot a tree showing the clustering relationships used to create the alignment. PILEUP uses a
10 simplification of the progressive alignment method of Feng & Doolittle, 1987, *J. Mol. Evol.* 35:351-360; the method is similar to that described by Higgins and Sharp, 1989, *CABIOS* 5:151-153. Useful PILEUP parameters including a default gap weight of 3.00, a default gap length weight of 0.10, and weighted end gaps.

Another example of a useful algorithm is the BLAST algorithm, described in: Altschul *et al.*,
15 1990, *J. Mol. Biol.* 215:403-410; Altschul *et al.*, 1997, *Nucleic Acids Res.* 25:3389-3402; and Karin *et al.*, 1993, *Proc. Natl. Acad. Sci. U.S.A.* 90:5873-5787. A particularly useful BLAST program is the WU-BLAST-2 program which was obtained from Altschul *et al.*, 1996, *Methods in Enzymology* 266:460-480. WU-BLAST-2 uses several search parameters, most of which are set to the default values. The adjustable parameters are set with the following
20 values: overlap span=1, overlap fraction=0.125, word threshold (T)=11. The HSP S and HSP S2 parameters are dynamic values and are established by the program itself depending upon the composition of the particular sequence and composition of the particular database against which the sequence of interest is being searched; however, the values may be adjusted to increase sensitivity.

An additional useful algorithm is gapped BLAST as reported by Altschul *et al.*, 1993, *Nucl. Acids Res.* 25:3389-3402. Gapped BLAST uses BLOSUM-62 substitution scores; threshold
25 T parameter set to 9; the two-hit method to trigger ungapped extensions, charges gap lengths of k a cost of 10+k; Xu set to 16, and Xg set to 40 for database search stage and to 67 for the output stage of the algorithms. Gapped alignments are triggered by a score
30 corresponding to about 22 bits.

Generally, the amino acid homology, similarity, or identity between individual variant CDRs are at least 80% to the sequences depicted herein, and more typically with preferably increasing homologies or identities of at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, and almost 100%. In a similar manner, "percent (%) nucleic acid sequence
35 identity" with respect to the nucleic acid sequence of the binding proteins identified herein is

defined as the percentage of nucleotide residues in a candidate sequence that are identical with the nucleotide residues in the coding sequence of the antigen binding protein. A specific method utilizes the BLASTN module of WU-BLAST-2 set to the default parameters, with overlap span and overlap fraction set to 1 and 0.125, respectively.

- 5 Generally, the nucleic acid sequence homology, similarity, or identity between the nucleotide sequences encoding individual variant CDRs and the nucleotide sequences depicted herein are at least 80%, and more typically with preferably increasing homologies or identities of at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, and almost 100%.
- 10 Thus, a "variant CDR" is one with the specified homology, similarity, or identity to the parent CDR of the invention, and shares biological function, including, but not limited to, at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the specificity and/or activity of the parent CDR.

- While the site or region for introducing an amino acid sequence variation is predetermined,
- 15 the mutation *per se* need not be predetermined. For example, in order to optimize the performance of a mutation at a given site, random mutagenesis may be conducted at the target codon or region and the expressed antigen binding protein CDR variants screened for the optimal combination of desired activity. Techniques for making substitution mutations at predetermined sites in DNA having a known sequence are well known, for example, M13
- 20 primer mutagenesis and PCR mutagenesis. Screening of the mutants is done using assays of antigen binding protein activities, such as binding to an elected a cell surface molecule on a target cell.

- The term "amino acid" or "amino acid residue" typically refers to an amino acid having its art recognized definition such as an amino acid selected from the group consisting of: alanine
- 25 (Ala or A); arginine (Arg or R); asparagine (Asn or N); aspartic acid (Asp or D); cysteine (Cys or C); glutamine (Gln or Q); glutamic acid (Glu or E); glycine (Gly or G); histidine (His or H); isoleucine (He or I); leucine (Leu or L); lysine (Lys or K); methionine (Met or M); phenylalanine (Phe or F); pro line (Pro or P); serine (Ser or S); threonine (Thr or T); tryptophan (Trp or W); tyrosine (Tyr or Y); and valine (Val or V), although modified, synthetic,
- 30 or rare amino acids may be used as desired. Generally, amino acids can be grouped as having a nonpolar side chain (e.g., Ala, Cys, He, Leu, Met, Phe, Pro, Val); a negatively charged side chain (e.g., Asp, Glu); a positively charged sidechain (e.g., Arg, His, Lys); or an uncharged polar side chain (e.g., Asn, Cys, Gln, Gly, His, Met, Phe, Ser, Thr, Trp, and Tyr).
- The term "hypervariable region" (also known as "complementarity determining regions" or
- 35 CDRs) when used herein refers to the amino acid residues of an antibody which are (usually

three or four short regions of extreme sequence variability) within the V-region domain of an immunoglobulin which form the antigen-binding site and are the main determinants of antigen specificity. There are at least two methods for identifying the CDR residues: (1) An approach based on cross-species sequence variability (i. e., Kabat *et al.*, loc. cit.); and (2) An approach based on crystallographic studies of antigen-antibody complexes (Chothia, C. *et al.*, J. Mol. Biol. 196: 901-917 (1987)). However, to the extent that two residue identification techniques define regions of overlapping, but not identical regions, they can be combined to define a hybrid CDR. However, in general, the CDR residues are preferably identified in accordance with the so-called Kabat (numbering) system.

The term "framework region" refers to the art-recognized portions of an antibody variable region that exist between the more divergent (i.e., hypervariable) CDRs. Such framework regions are typically referred to as frameworks 1 through 4 (FR1, FR2, FR3, and FR4) and provide a scaffold for the presentation of the six CDRs (three from the heavy chain and three from the light chain) in three dimensional space, to form an antigen-binding surface.

Typically, CDRs form a loop structure that can be classified as a canonical structure. The term "canonical structure" refers to the main chain conformation that is adopted by the antigen binding (CDR) loops. From comparative structural studies, it has been found that five of the six antigen binding loops have only a limited repertoire of available conformations. Each canonical structure can be characterized by the torsion angles of the polypeptide backbone. Correspondent loops between antibodies may, therefore, have very similar three dimensional structures, despite high amino acid sequence variability in most parts of the loops (Chothia and Lesk, J. Mol. Biol., 1987, 196: 901; Chothia *et al.*, Nature, 1989, 342: 877; Martin and Thornton, J. Mol. Biol, 1996, 263: 800, each of which is incorporated by reference in its entirety). Furthermore, there is a relationship between the adopted loop structure and the amino acid sequences surrounding it. The conformation of a particular canonical class is determined by the length of the loop and the amino acid residues residing at key positions within the loop, as well as within the conserved framework (i.e., outside of the loop). Assignment to a particular canonical class can therefore be made based on the presence of these key amino acid residues. The term "canonical structure" may also include considerations as to the linear sequence of the antibody, for example, as catalogued by Kabat (Kabat *et al.*, loc. cit.). The Kabat numbering scheme (system) is a widely adopted standard for numbering the amino acid residues of an antibody variable domain in a consistent manner and is the preferred scheme applied in the present invention as also mentioned elsewhere herein. Additional structural considerations can also be used to determine the canonical structure of an antibody. For example, those differences not fully reflected by Kabat numbering can be described by the numbering system of Chothia *et al* and/or revealed by other techniques, for example, crystallography and two or three-

dimensional computational modeling. Accordingly, a given antibody sequence may be placed into a canonical class which allows for, among other things, identifying appropriate chassis sequences (e.g., based on a desire to include a variety of canonical structures in a library). Kabat numbering of antibody amino acid sequences and structural considerations as described by Chothia *et al.*, loc. cit. and their implications for construing canonical aspects of antibody structure, are described in the literature.

CDR3 is typically the greatest source of molecular diversity within the antibody-binding site. H3, for example, can be as short as two amino acid residues or greater than 26 amino acids. The subunit structures and three-dimensional configurations of different classes of immunoglobulins are well known in the art. For a review of the antibody structure, see Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, eds. Harlow *et al.*, 1988. One of skill in the art will recognize that each subunit structure, e.g., a CH, VH, CL, VL, CDR, FR structure, comprises active fragments, e.g., the portion of the VH, VL, or CDR subunit that binds to the antigen, i.e., the antigen-binding fragment, or, e.g., the portion of the CH subunit that binds to and/or activates, e.g., an Fc receptor and/or complement. The CDRs typically refer to the Kabat CDRs, as described in Sequences of Proteins of immunological Interest, US Department of Health and Human Services (1991), eds. Kabat *et al.* Another standard for characterizing the antigen binding site is to refer to the hypervariable loops as described by Chothia. See, e.g., Chothia, *et al.* (1987; J. Mol. Biol. 227:799-817); and Tomlinson *et al.* (1995) EMBO J. 14: 4628-4638. Still another standard is the AbM definition used by Oxford Molecular's AbM antibody modeling software. See, generally, e.g., Protein Sequence and Structure Analysis of Antibody Variable Domains. In: Antibody Engineering Lab Manual (Ed.: Duebel, S. and Kontermann, R., Springer-Verlag, Heidelberg). Embodiments described with respect to Kabat CDRs can alternatively be implemented using similar described relationships with respect to Chothia hypervariable loops or to the AbM-defined loops.

The sequence of antibody genes after assembly and somatic mutation is highly varied, and these varied genes are estimated to encode 10^{10} different antibody molecules (Immunoglobulin Genes, 2nd ed., eds. Jonio *et al.*, Academic Press, San Diego, CA, 1995). Accordingly, the immune system provides a repertoire of immunoglobulins. The term "repertoire" refers to at least one nucleotide sequence derived wholly or partially from at least one sequence encoding at least one immunoglobulin. The sequence(s) may be generated by rearrangement in vivo of the V, D, and J segments of heavy chains, and the V and J segments of light chains. Alternatively, the sequence(s) can be generated from a cell in response to which rearrangement occurs, e.g., in vitro stimulation. Alternatively, part or all of the sequence(s) may be obtained by DNA splicing, nucleotide synthesis, mutagenesis, and other methods, see, e.g., U.S. Patent 5,565,332. A repertoire may include only one

sequence or may include a plurality of sequences, including ones in a genetically diverse collection.

It is also envisaged that the CD33 targeting compound described herein has, apart from its function to bind to the cell surface molecule CD33 on a target cell and CD3 on the cell surface of a T cell, may have an additional function. In this format, the compound is a multifunctional compound by targeting cells through binding to CD33 on the cell surface of a target cell, mediating cytotoxic T cell activity through CD3 binding and providing a further function such as a fully functional Fc constant domain mediating antibody-dependent cellular cytotoxicity through recruitment of effector cells like NK cells, a half life extending domain such as an albumin binding domain or a modified Fc constant domain lacking antibody-dependent cellular cytotoxicity but extending the molecular weight of the compound, mediation of a label (fluorescent etc.), a therapeutic agent such as, e.g. a toxin or radionuclide, and/or means to enhance serum half-life, etc.

The term "epitope" refers to a site on an antigen to which a binding domain, such as an antibody or immunoglobulin or derivative or fragment of an antibody or of an immunoglobulin, specifically binds. An "epitope" is antigenic and thus the term epitope is sometimes also referred to herein as "antigenic structure" or "antigenic determinant". Thus, the binding domain is an "antigen-interaction-site". Said binding/interaction is also understood to define a "specific recognition". In one example, said binding domain which (specifically) binds to / interacts with a given target epitope of CD33 on a cell surface molecule on a target cell or CD3 is an antibody or immunoglobulin, and said binding domain is a VH and/or VL region of an antibody or of an immunoglobulin.

"Epitopes" can be formed both by contiguous amino acids or non-contiguous amino acids juxtaposed by tertiary folding of a protein. A "linear epitope" is an epitope where an amino acid primary sequence comprises the recognized epitope. A linear epitope typically includes at least 3 or at least 4, and more usually, at least 5 or at least 6 or at least 7, for example, about 8 to about 10 amino acids in a unique sequence.

A "conformational epitope", in contrast to a linear epitope, is an epitope wherein the primary sequence of the amino acids comprising the epitope is not the sole defining component of the epitope recognized (e.g., an epitope wherein the primary sequence of amino acids is not necessarily recognized by the binding domain). Typically a conformational epitope comprises an increased number of amino acids relative to a linear epitope. With regard to recognition of conformational epitopes, the binding domain recognizes a three-dimensional structure of the antigen, preferably a peptide or protein or fragment thereof (in the context of the present invention, the antigen for one of the binding domains is comprised within a cell surface molecule on a target cell). For example, when a protein molecule folds to form a

three-dimensional structure, certain amino acids and/or the polypeptide backbone forming the conformational epitope become juxtaposed enabling the antibody to recognize the epitope. Methods of determining the conformation of epitopes include, but are not limited to, x-ray crystallography, two-dimensional nuclear magnetic resonance (2D-NMR) spectroscopy and site-directed spin labelling and electron paramagnetic resonance (EPR) spectroscopy. Moreover, the provided examples describe a further method to characterize a given binding domain by way of binning, which includes a test whether the given binding domain binds to one or more epitope cluster(s) of a given protein, in particular a cell surface molecule on a target cell.

As used herein, the term "epitope cluster" denotes the entirety of epitopes lying in a defined contiguous stretch of an antigen. An epitope cluster can comprise one, two or more epitopes. The concept of epitope cluster is also used in the characterization of the features of the binding molecules of the invention.

The terms "(capable of) binding to", "specifically recognizing", "directed to" and "reacting with" mean in accordance with this invention that a binding domain is capable of specifically interacting with one or more, preferably at least two, more preferably at least three and most preferably at least four amino acids of an epitope.

As used herein, the terms "specifically interacting", "specifically binding" or "specifically bind(s)" mean that a binding domain exhibits appreciable affinity for a particular protein or antigen and, generally, does not exhibit significant reactivity with proteins or antigens other than CD33 or CD3. "Appreciable affinity" includes binding with an affinity of about 10^{-6} M (KD) or stronger. Preferably, binding is considered specific when binding affinity is about 10^{-12} to 10^{-8} M, 10^{-12} to 10^{-9} M, 10^{-12} to 10^{-10} M, 10^{-11} to 10^{-8} M, preferably of about 10^{-11} to 10^{-9} M. Whether a binding domain specifically reacts with or binds to a target can be tested readily by, *inter alia*, comparing the reaction of said binding domain with a target protein or antigen with the reaction of said binding domain with proteins or antigens other than CD33 or CD3. Preferably, a binding domain of the invention does not essentially bind or is not capable of binding to proteins or antigens other than CD33 or CD3 (i.e. the first binding domain is not capable of binding to proteins other than CD33 and the second binding domain is not capable of binding to proteins other than CD3).

The term "does not essentially bind", or "is not capable of binding" means that a binding domain of the present invention does not bind another protein or antigen other than CD33 or CD3, i.e., does not show reactivity of more than 30%, preferably not more than 20%, more preferably not more than 10%, particularly preferably not more than 9%, 8%, 7%, 6% or 5%

with proteins or antigens other than CD33 or CD3, whereby binding to CD33 or CD3, respectively, is set to be 100%.

Specific binding is believed to be effected by specific motifs in the amino acid sequence of the binding domain and the antigen. Thus, binding is achieved as a result of their primary, secondary and/or tertiary structure as well as the result of secondary modifications of said structures. The specific interaction of the antigen-interaction-site with its specific antigen may result in a simple binding of said site to the antigen. Moreover, the specific interaction of the antigen-interaction-site with its specific antigen may alternatively or additionally result in the initiation of a signal, e.g. due to the induction of a change of the conformation of the antigen, an oligomerization of the antigen, etc.

Proteins (including fragments thereof, preferably biologically active fragments, and peptides, usually having less than 30 amino acids) comprise one or more amino acids coupled to each other via a covalent peptide bond (resulting in a chain of amino acids). The term "polypeptide" as used herein describes a group of molecules, which consist of more than 30 amino acids. Polypeptides may further form multimers such as dimers, trimers and higher oligomers, i.e. consisting of more than one polypeptide molecule. Polypeptide molecules forming such dimers, trimers etc. may be identical or non-identical. The corresponding higher order structures of such multimers are, consequently, termed homo- or heterodimers, homo- or heterotrimers etc. An example for a heteromultimer is an antibody molecule, which, in its naturally occurring form, consists of two identical light polypeptide chains and two identical heavy polypeptide chains. The terms "polypeptide" and "protein" also refer to naturally modified polypeptides/proteins wherein the modification is effected e.g. by post-translational modifications like glycosylation, acetylation, phosphorylation and the like. A "polypeptide" when referred to herein may also be chemically modified such as pegylated. Such modifications are well known in the art.

"Isolated" when used to describe the CD33 targeting compound disclosed herein, means a compound that has been identified, separated and/or recovered from a component of its production environment. Preferably, the isolated compound is free of association with all other components from its production environment. Contaminant components of its production environment, such as that resulting from recombinant transfected cells, are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In preferred embodiments, the compound will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-

reducing or reducing conditions using Coomassie blue or, preferably, silver stain. Ordinarily, however, an isolated compound will be prepared by at least one purification step.

Amino acid sequence modifications of the CD33 targeting compound described herein are contemplated. For example, it may be desirable to improve the binding affinity and/or other biological properties of the compound. Amino acid sequence variants of the CD33 targeting compounds are prepared by introducing appropriate nucleotide changes into the compounds nucleic acid, or by peptide synthesis.

Such modifications include, for example, deletions from, and/or insertions into, and/or substitutions of, residues within the amino acid sequences of the compound. Any combination of deletion, insertion, and substitution is made to arrive at the final construct, provided that the final construct possesses the desired characteristics. The amino acid changes also may alter post-translational processes of the compound, such as changing the number or position of glycosylation sites. Preferably, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids may be substituted in a CDR, while 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 25 amino acids may be substituted in the framework regions (FRs). The substitutions are preferably conservative substitutions as described herein. Additionally or alternatively, 1, 2, 3, 4, 5, or 6 amino acids may be inserted or deleted in each of the CDRs (of course, dependent on their length), while 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 25 amino acids may be inserted or deleted in each of the FRs.

A useful method for identification of certain residues or regions of the CD33 targeting compounds that are preferred locations for mutagenesis is called "alanine scanning mutagenesis" as described by Cunningham and Wells in *Science*, 244: 1081-1085 (1989). Here, a residue or group of target residues within the compound is/are identified (e.g. charged residues such as arg, asp, his, lys, and glu) and replaced by a neutral or negatively charged amino acid (most preferably alanine or polyalanine) to affect the interaction of the amino acids with the epitope.

Those amino acid locations demonstrating functional sensitivity to the substitutions then are refined by introducing further or other variants at, or for, the sites of substitution. Thus, while the site for introducing an amino acid sequence variation is predetermined, the nature of the mutation *per se* needs not to be predetermined. For example, to analyze the performance of a mutation at a given site, ala scanning or random mutagenesis is conducted at a target codon or region and the expressed compound variants are screened for the desired activity.

Preferably, amino acid sequence insertions include amino- and/or carboxyl-terminal fusions ranging in length from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 residues to polypeptides containing a hundred or more residues, as well as intrasequence insertions of single or multiple amino

acid residues. An insertional variant of the CD33 targeting compound includes the fusion to the N-or C-terminus of the antibody to an enzyme or a fusion to a polypeptide which increases the serum half-life of the antibody.

Another type of variant is an amino acid substitution variant. These variants have preferably at least 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid residues in the compound replaced by a different residue. The sites of greatest interest for substitutional mutagenesis include the CDRs of the heavy and/or light chain, in particular the hypervariable regions, but FR alterations in the heavy and/or light chain are also contemplated.

For example, if a CDR sequence encompasses 6 amino acids, it is envisaged that one, two or three of these amino acids are substituted. Similarly, if a CDR sequence encompasses 15 amino acids it is envisaged that one, two, three, four, five or six of these amino acids are substituted.

Generally, if amino acids are substituted in one or more or all of the CDRs of the heavy and/or light chain, it is preferred that the then-obtained "substituted" sequence is at least 60%, more preferably 65%, even more preferably 70%, particularly preferably 75%, more particularly preferably 80% identical to the "original" CDR sequence. This means that it is dependent of the length of the CDR to which degree it is identical to the "substituted" sequence. For example, a CDR having 5 amino acids is preferably 80% identical to its substituted sequence in order to have at least one amino acid substituted. Accordingly, the CDRs of the CD33 targeting compound may have different degrees of identity to their substituted sequences, e.g., CDRL1 may have 80%, while CDRL3 may have 90%.

Preferred substitutions (or replacements) are conservative substitutions. However, any substitution (including non-conservative substitution or one or more from the "exemplary substitutions" listed in Table 1, below) is envisaged as long as the CD33 targeting compound retains its capability to bind to CD33 via the first binding domain and to CD3 epsilon via the second binding domain and/or its CDRs have an identity to the then substituted sequence (at least 60%, more preferably 65%, even more preferably 70%, particularly preferably 75%, more particularly preferably 80% identical to the "original" CDR sequence).

Conservative substitutions are shown in Table 1 under the heading of "preferred substitutions". If such substitutions result in a change in biological activity, then more substantial changes, denominated "exemplary substitutions" in Table 1, or as further described below in reference to amino acid classes, may be introduced and the products screened for a desired characteristic.

Table 1: Amino Acid Substitutions

Original	Exemplary Substitutions	Preferred Substitutions
Ala (A)	val, leu, ile	val
Arg (R)	lys, gln, asn	lys
Asn (N)	gln, his, asp, lys, arg	gln
Asp (D)	glu, asn	glu
Cys (C)	ser, ala	ser
Gln (Q)	asn, glu	asn
Glu (E)	asp, gln	asp
Gly (G)	ala	ala
His (H)	asn, gln, lys, arg	arg
Ile (I)	leu, val, met, ala, phe	leu
Leu (L)	norleucine, ile, val, met, ala	ile
Lys (K)	arg, gln, asn	arg
Met (M)	leu, phe, ile	leu
Phe (F)	leu, val, ile, ala, tyr	tyr
Pro (P)	ala	ala
Ser (S)	thr	thr
Thr (T)	ser	ser
Trp (W)	tyr, phe	tyr
Tyr (Y)	trp, phe, thr, ser	phe
Val (V)	ile, leu, met, phe, ala	leu

Substantial modifications in the biological properties of the CD33 targeting compound described herein are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side-chain properties: (1) hydrophobic: norleucine, met, ala, val, leu, ile; (2) neutral hydrophilic: cys, ser, thr; (3) acidic: asp, glu; (4) basic: asn, gin, his, lys, arg; (5) residues that influence chain orientation: gly, pro; and (6) aromatic : trp, tyr, phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class. Any cysteine residue not involved in maintaining the proper conformation of the CD33 targeting compound may be substituted, generally with serine, to improve the oxidative stability of the molecule and prevent aberrant crosslinking. Conversely, cysteine

bond(s) may be added to the compound in case the compound is an antibody to improve its stability (particularly where the antibody is an antibody fragment such as an Fv fragment).

A particularly preferred type of substitutional variant involves substituting one or more hypervariable region residues of a parent antibody (e. g. a humanized or human antibody).

5 Generally, the resulting variant(s) selected for further development will have improved biological properties relative to the parent antibody from which they are generated. A convenient way for generating such substitutional variants involves affinity maturation using phage display. Briefly, several hypervariable region sites (e. g. 6-7 sites) are mutated to generate all possible amino acid substitutions at each site. The antibody variants thus
10 generated are displayed in a monovalent fashion from filamentous phage particles as fusions to the gene III product of M13 packaged within each particle. The phage-displayed variants are then screened for their biological activity (e. g. binding affinity) as herein disclosed. In order to identify candidate hypervariable region sites for modification, alanine scanning mutagenesis can be performed to identify hypervariable region residues
15 contributing significantly to antigen binding. Alternatively, or additionally, it may be beneficial to analyze a crystal structure of the antigen-antibody complex to identify contact points between the binding domain and, e.g., human CD33 or CD3. Such contact residues and neighbouring residues are candidates for substitution according to the techniques elaborated herein. Once such variants are generated, the panel of variants is subjected to screening as
20 described herein and antibodies with superior properties in one or more relevant assays may be selected for further development.

Other modifications of the CD33 targeting compound are contemplated herein. For example, the CD33 targeting compound may be linked to one of a variety of non-proteinaceous polymers, e.g., polyethylene glycol, polypropylene glycol, polyoxyalkylenes, or copolymers of
25 polyethylene glycol and polypropylene glycol. The CD33 targeting compound may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization (for example, hydroxymethylcellulose or gelatine-microcapsules and poly (methylmethacrylate) microcapsules, respectively), in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nanoparticles and
30 nanocapsules), or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences, 16th edition, Oslo, A., Ed., (1980).

The CD33 targeting compound disclosed herein may also be formulated as immuno-liposomes. A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant which is useful for delivery of a drug to a mammal. The components of the
35 liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of biological membranes. Liposomes containing the compound are prepared by methods

known in the art, such as described in Epstein *et al.*, Proc. Natl. Acad. Sci. USA, 82: 3688 (1985); Hwang *et al.*, Proc. Natl. Acad. Sci. USA, 77: 4030 (1980); US Pat. Nos. 4,485,045 and 4,544,545; and W0 97/38731 published October 23, 1997. Liposomes with enhanced circulation time are disclosed in US Patent No. 5,013, 556. Particularly useful liposomes can be generated by the reverse phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin *et al.* J. Biol. Chem. 257: 286-288 (1982) via a disulfide interchange reaction. A chemotherapeutic agent is optionally contained within the liposome. See Gabizon *et al.* J. National Cancer Inst. 81 (19) 1484 (1989).

When using recombinant techniques, the CD33 targeting compound can be produced intracellularly, in the periplasmic space, or directly secreted into the medium. If the antibody construct is produced intracellularly, as a first step, the particulate debris, either host cells or lysed fragments, are removed, for example, by centrifugation or ultrafiltration. Carter *et al.*, Bio/Technology 10: 163-167 (1992) describe a procedure for isolating antibodies which are secreted to the periplasmic space of *E. coli*.

The CD33 targeting compounds prepared from the cells can be purified using, for example, hydroxylapatite chromatography, gel electrophoresis, dialysis, and affinity chromatography, with affinity chromatography being the preferred purification technique.

The CD33 targeting compounds described herein may be provided in form of a fusion protein comprising at least two binding domains, with or without peptide linkers (spacer peptides). Among the suitable peptide linkers are those described in U.S. Patents 4,751,180 and 4,935,233 or WO 88/09344.

Another method for preparing CD33 targeting compounds described herein in form of oligomeric antibody construct derivatives involves use of a leucine zipper. Leucine zipper domains are peptides that promote oligomerization of the proteins in which they are found. Leucine zippers were originally identified in several DNA-binding proteins (Landschulz *et al.*, 1988, *Science* 240:1759), and have since been found in a variety of different proteins. Among the known leucine zippers are naturally occurring peptides and derivatives thereof that dimerize or trimerize. Examples of leucine zipper domains suitable for producing soluble oligomeric proteins are described in PCT application WO 94/10308, and the leucine zipper derived from lung surfactant protein D (SPD) described in Hoppe *et al.*, 1994, *FEBS Letters* 344:191, hereby incorporated by reference. The use of a modified leucine zipper that allows for stable trimerization of a heterologous protein fused thereto is described in Fanslow *et al.*,

1994, *Semin. Immunol.* 6:267-78. In one approach, recombinant fusion proteins comprising a CD33 and a CD3 antibody fragment or derivative fused to a leucine zipper peptide are expressed in suitable host cells, and the soluble oligomeric CD33 and CD3 antibody fragments or derivatives that form are recovered from the culture supernatant.

- 5 Covalent modifications of antigen binding proteins are included within the scope of this invention, and are generally, but not always, done post-translationally. For example, several types of covalent modifications of the antigen binding protein are introduced into the molecule by reacting specific amino acid residues of the antigen binding protein with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or
10 C-terminal residues.

Cysteiny l residues most commonly are reacted with α -haloacetates (and corresponding amines), such as chloroacetic acid or chloroacetamide, to give carboxymethyl or carboxyamidomethyl derivatives. Cysteiny l residues also are derivatized by reaction with
15 bromotrifluoroacetone, α -bromo- β -(5-imidazolyl)propionic acid, chloroacetyl phosphate, N-alkylmaleimides, 3-nitro-2-pyridyl disulfide, methyl 2-pyridyl disulfide, p-chloromercuribenzoate, 2-chloromercuri-4-nitrophenol, or chloro-7-nitrobenzo-2-oxa-1,3-diazole.

Histidyl residues are derivatized by reaction with diethylpyrocarbonate at pH 5.5-7.0 because this agent is relatively specific for the histidyl side chain. Para-bromophenacyl bromide also
20 is useful; the reaction is preferably performed in 0.1M sodium cacodylate at pH 6.0.

Lysiny l and amino terminal residues are reacted with succinic or other carboxylic acid anhydrides. Derivatization with these agents has the effect of reversing the charge of the lysiny l residues. Other suitable reagents for derivatizing alpha-amino-containing residues include imidoesters such as methyl picolinimidate; pyridoxal phosphate; pyridoxal;
25 chloroborohydride; trinitrobenzenesulfonic acid; O-methylisourea; 2,4-pentanedione; and transaminase-catalyzed reaction with glyoxylate.

Arginy l residues are modified by reaction with one or several conventional reagents, among them phenylglyoxal, 2,3-butanedione, 1,2-cyclohexanedione, and ninhydrin. Derivatization of arginine residues requires that the reaction be performed in alkaline conditions because of
30 the high pKa of the guanidine functional group. Furthermore, these reagents may react with the groups of lysine as well as the arginine epsilon-amino group.

The specific modification of tyrosyl residues may be made, with particular interest in introducing spectral labels into tyrosyl residues by reaction with aromatic diazonium compounds or tetranitromethane. Most commonly, N-acetylimidazole and tetranitromethane
35 are used to form O-acetyl tyrosyl species and 3-nitro derivatives, respectively. Tyrosyl

residues are iodinated using ^{125}I or ^{131}I to prepare labeled proteins for use in radioimmunoassay, the chloramine T method described above being suitable.

Carboxyl side groups (aspartyl or glutamyl) are selectively modified by reaction with carbodiimides ($\text{R}'\text{---N}=\text{C}=\text{N}\text{---R}'$), where R and R' are optionally different alkyl groups, such as 1-cyclohexyl-3-(2-morpholinyl-4-ethyl) carbodiimide or 1-ethyl-3-(4-azonia-4,4-dimethylpentyl) carbodiimide. Furthermore, aspartyl and glutamyl residues are converted to asparaginyl and glutaminyl residues by reaction with ammonium ions.

Derivatization with bifunctional agents is useful for crosslinking antigen binding proteins to a water-insoluble support matrix or surface for use in a variety of methods. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), and bifunctional maleimides such as bis-N-maleimido-1,8-octane. Derivatizing agents such as methyl-3-[(p-azidophenyl)dithio]propioimide yield photoactivatable intermediates that are capable of forming crosslinks in the presence of light. Alternatively, reactive water-insoluble matrices such as cyanogen bromide-activated carbohydrates and the reactive substrates described in U.S. Pat. Nos. 3,969,287; 3,691,016; 4,195,128; 4,247,642; 4,229,537; and 4,330,440 are employed for protein immobilization.

Glutaminyl and asparaginyl residues are frequently deamidated to the corresponding glutamyl and aspartyl residues, respectively. Alternatively, these residues are deamidated under mildly acidic conditions. Either form of these residues falls within the scope of this invention.

Other modifications include hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, methylation of the α -amino groups of lysine, arginine, and histidine side chains (T. E. Creighton, *Proteins: Structure and Molecular Properties*, W. H. Freeman & Co., San Francisco, 1983, pp. 79-86), acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

Another type of covalent modification of the antigen binding protein included within the scope of this invention comprises altering the glycosylation pattern of the protein. As is known in the art, glycosylation patterns can depend on both the sequence of the protein (e.g., the presence or absence of particular glycosylation amino acid residues, discussed below), or the host cell or organism in which the protein is produced. Particular expression systems are discussed below.

Glycosylation of polypeptides is typically either N-linked or O-linked. N-linked refers to the attachment of the carbohydrate moiety to the side chain of an asparagine residue. The tri-

peptide sequences asparagine-X-serine and asparagine-X-threonine, where X is any amino acid except proline, are the recognition sequences for enzymatic attachment of the carbohydrate moiety to the asparagine side chain. Thus, the presence of either of these tri-peptide sequences in a polypeptide creates a potential glycosylation site. O-linked glycosylation refers to the attachment of one of the sugars N-acetylgalactosamine, galactose, or xylose, to a hydroxyamino acid, most commonly serine or threonine, although 5-hydroxyproline or 5-hydroxylysine may also be used.

Addition of glycosylation sites to the antigen binding protein is conveniently accomplished by altering the amino acid sequence such that it contains one or more of the above-described tri-peptide sequences (for N-linked glycosylation sites). The alteration may also be made by the addition of, or substitution by, one or more serine or threonine residues to the starting sequence (for O-linked glycosylation sites). For ease, the antigen binding protein amino acid sequence is preferably altered through changes at the DNA level, particularly by mutating the DNA encoding the target polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

Another means of increasing the number of carbohydrate moieties on the antigen binding protein is by chemical or enzymatic coupling of glycosides to the protein. These procedures are advantageous in that they do not require production of the protein in a host cell that has glycosylation capabilities for N- and O-linked glycosylation. Depending on the coupling mode used, the sugar(s) may be attached to (a) arginine and histidine, (b) free carboxyl groups, (c) free sulfhydryl groups such as those of cysteine, (d) free hydroxyl groups such as those of serine, threonine, or hydroxyproline, (e) aromatic residues such as those of phenylalanine, tyrosine, or tryptophan, or (f) the amide group of glutamine. These methods are described in WO 87/05330 published Sep. 11, 1987, and in Aplin and Wriston, 1981, *CRC Crit. Rev. Biochem.*, pp. 259-306.

Removal of carbohydrate moieties present on the starting antigen binding protein may be accomplished chemically or enzymatically. Chemical deglycosylation requires exposure of the protein to the compound trifluoromethanesulfonic acid, or an equivalent compound. This treatment results in the cleavage of most or all sugars except the linking sugar (N-acetylglucosamine or N-acetylgalactosamine), while leaving the polypeptide intact. Chemical deglycosylation is described by Hakimuddin *et al.*, 1987, *Arch. Biochem. Biophys.* 259:52 and by Edge *et al.*, 1981, *Anal. Biochem.* 118:131. Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo- and exo-glycosidases as described by Thotakura *et al.*, 1987, *Meth. Enzymol.* 138:350. Glycosylation at potential glycosylation sites may be prevented by the use of the compound tunicamycin as

described by Duskin *et al.*, 1982, *J. Biol. Chem.* 257:3105. Tunicamycin blocks the formation of protein-N-glycoside linkages.

Another type of covalent modification of the antigen binding protein comprises linking the antigen binding protein to various non-proteinaceous polymers, including, but not limited to, various polyols such as polyethylene glycol, polypropylene glycol or polyoxyalkylenes, in the manner set forth in U.S. Pat. Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337. In addition, as is known in the art, amino acid substitutions may be made in various positions within the antigen binding protein to facilitate the addition of polymers such as PEG.

- 10 In some embodiments, the covalent modification of the antigen binding proteins described herein comprises the addition of one or more labels.

The term "labelling group" means any detectable label. Examples of suitable labelling groups include, but are not limited to, the following: radioisotopes or radionuclides (*e.g.*, ^3H , ^{14}C , ^{15}N , ^{35}S , ^{90}Y , ^{99}Tc , ^{111}In , ^{125}I , ^{131}I), fluorescent groups (*e.g.*, FITC, rhodamine, lanthanide phosphors), enzymatic groups (*e.g.*, horseradish peroxidase, β -galactosidase, luciferase, alkaline phosphatase), chemiluminescent groups, biotinyl groups, or predetermined polypeptide epitopes recognized by a secondary reporter (*e.g.*, leucine zipper pair sequences, binding sites for secondary antibodies, metal binding domains, epitope tags). In some embodiments, the labelling group is coupled to the antigen binding protein *via* spacer arms of various lengths to reduce potential steric hindrance. Various methods for labelling proteins are known in the art and may be used in performing the present invention.

In general, labels fall into a variety of classes, depending on the assay in which they are to be detected: a) isotopic labels, which may be radioactive or heavy isotopes; b) magnetic labels (*e.g.*, magnetic particles); c) redox active moieties; d) optical dyes; enzymatic groups (*e.g.* horseradish peroxidase, β -galactosidase, luciferase, alkaline phosphatase); e) biotinylated groups; and f) predetermined polypeptide epitopes recognized by a secondary reporter (*e.g.*, leucine zipper pair sequences, binding sites for secondary antibodies, metal binding domains, epitope tags, etc.). In some embodiments, the labelling group is coupled to the antigen binding protein *via* spacer arms of various lengths to reduce potential steric hindrance. Various methods for labelling proteins are known in the art and may be used in performing the present invention.

Specific labels include optical dyes, including, but not limited to, chromophores, phosphors and fluorophores, with the latter being specific in many instances. Fluorophores can be either "small molecule" fluo- res, or proteinaceous fluo- res.

By "fluorescent label" is meant any molecule that may be detected via its inherent fluorescent properties. Suitable fluorescent labels include, but are not limited to, fluorescein, rhodamine, tetramethylrhodamine, eosin, erythrosin, coumarin, methyl-coumarins, pyrene, Malacite green, stilbene, Lucifer Yellow, Cascade BlueJ, Texas Red, IAEDANS, EDANS, BODIPY FL, LC Red 640, Cy 5, Cy 5.5, LC Red 705, Oregon green, the Alexa-Fluor dyes (Alexa Fluor 350, Alexa Fluor 430, Alexa Fluor 488, Alexa Fluor 546, Alexa Fluor 568, Alexa Fluor 594, Alexa Fluor 633, Alexa Fluor 660, Alexa Fluor 680), Cascade Blue, Cascade Yellow and R-phycoerythrin (PE) (Molecular Probes, Eugene, OR), FITC, Rhodamine, and Texas Red (Pierce, Rockford, IL), Cy5, Cy5.5, Cy7 (Amersham Life Science, Pittsburgh, PA). Suitable optical dyes, including fluorophores, are described in Molecular Probes Handbook by Richard P. Haugland, hereby expressly incorporated by reference.

Suitable proteinaceous fluorescent labels also include, but are not limited to, green fluorescent protein, including a Renilla, Ptilosarcus, or Aequorea species of GFP (Chalfie *et al.*, 1994, *Science* 263:802-805), EGFP (Clontech Laboratories, Inc., Genbank Accession Number U55762), blue fluorescent protein (BFP, Quantum Biotechnologies, Inc. 1801 de Maisonneuve Blvd. West, 8th Floor, Montreal, Quebec, Canada H3H 1J9; Stauber, 1998, *Biotechniques* 24:462-471; Heim *et al.*, 1996, *Curr. Biol.* 6:178-182), enhanced yellow fluorescent protein (EYFP, Clontech Laboratories, Inc.), luciferase (Ichiki *et al.*, 1993, *J. Immunol.* 150:5408-5417), β galactosidase (Nolan *et al.*, 1988, *Proc. Natl. Acad. Sci. U.S.A.* 85:2603-2607) and Renilla (WO92/15673, WO95/07463, WO98/14605, WO98/26277, WO99/49019, U.S. Patent Nos. 5292658, 5418155, 5683888, 5741668, 5777079, 5804387, 5874304, 5876995, 5925558). All of the above-cited references are expressly incorporated herein by reference.

A CD33 targeting compound described herein may also comprise additional domains, which e.g. are helpful in the isolation of the molecule or relate to an adapted pharmacokinetic profile of the molecule.

Domains helpful for the isolation of an antibody construct may be elected from peptide motives or secondarily introduced moieties, which can be captured in an isolation method, e.g. an isolation column. A non-limiting embodiments of such additional domains comprise peptide motives known as Myc-tag, HAT-tag, HA-tag, TAP-tag, GST-tag, chitin binding domain (CBD-tag), maltose binding protein (MBP-tag), Flag-tag, Strep-tag and variants thereof (e.g. StrepII-tag) and His-tag. All herein disclosed antibody constructs characterized by the identified CDRs are preferred to comprise a His-tag domain, which is generally known as a repeat of consecutive His residues in the amino acid sequence of a molecule, preferably of six His residues.

The term "epigenetic factor" in connection with the present invention defines a compound which is capable of changing the gene expression or cellular phenotype of a cell population upon administration. It is understood that such change refers to one or more functional relevant modifications to the genome without involving a change in the nucleic acid sequence. Examples of such modifications are DNA methylation and histone modification, which are both important for the regulation of gene expression without altering the underlying DNA sequence. Particular examples for epigenetic factors suitable in the combination therapy approach according to the invention are selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors, hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone demethylase inhibitors and ATRA (All Trans-retinoic acid).

Histone deacetylases (HDACs) are a class of enzymes, that remove acetyl groups from ϵ -N-acetyl lysine amino acid on a histone. The deacetylated histone is suitable to wrap the DNA more tightly which negatively effects the expression genes in the region of the wrapped DNA. Accordingly, HDAC inhibitors inhibit the enzymatic deacetylation of histone and allow for the expression or enhancement of expression of those genes located in the region of the acetylated histone. Non-limiting examples for HDAC inhibitors in connection with this invention comprise panobinostat, vorinostat, romidepsin, N-acetyldinaline, belinostat, givinostat, entinostat, mocetinostat, EVP-0334, SRT501, CUDC-101, Quisinostat, abexinostat, LAQ824, and valproic acid.

DNA methyltransferase (DNMT) I is an enzyme, which catalyze the transfer of a methyl group to DNA. The degree of DNA methylation is also decisive for the expression of genes. Non-limiting examples for DNMT I inhibitors in connection with this invention comprise 5-azacitidine, decitabine, hydralazine, zebularine, procainamide, (-)-epigallocatechin-3-gallate, MG98, RG108, and SGI-110.

Histone methyltransferases (HMT) are histone-modifying enzymes that catalyze the transfer of one, two, or three methyl groups to lysine and arginine residues of histone proteins. Methylation of histones is important biologically because it is the principal epigenetic modification of chromatin that determines gene expression, genomic stability, stem cell maturation, cell lineage development, genetic imprinting, DNA methylation, and cell mitosis. Non-limiting examples for HMT inhibitors in connection with this invention comprise LSD1 (KDM1A) demethylase inhibitor, and chaetocin.

ATRA (All Trans-retinoic acid) is the carboxylic acid form of vitamin A and is also known as Tretinoin.

Hydroxyurea is also known as Hydroxycarbamide and is used as an antineoplastic drug. The compound is described to decrease the production of deoxyribonucleotides via inhibition of the enzyme ribonucleotide reductase.

Granulocyte-colony stimulating factor (G-CSF or GCSF), also known as colony-stimulating factor 3 (CSF 3), is a glycoprotein that stimulates the bone marrow to produce granulocytes and stem cells and release them into the bloodstream. Functionally, it is a cytokine and hormone, a type of colony-stimulating factor, and is produced by a number of different tissues. The pharmaceutical analogs of naturally occurring G-CSF are called filgrastim and lenograstim.

The term "nucleic acid" is well known to the skilled person and encompasses DNA (such as cDNA) and RNA (such as mRNA). The nucleic acid can be double stranded and single stranded, linear and circular. Said nucleic acid molecule is preferably comprised in a vector which is preferably comprised in a host cell. Said host cell is, e.g. after transformation or transfection with the nucleic acid sequence described herein, capable of expressing the CD33 targeting compound. For that purpose the nucleic acid molecule is operatively linked with control sequences.

A vector is a nucleic acid molecule used as a vehicle to transfer (foreign) genetic material into a cell. The term "vector" encompasses – but is not restricted to – plasmids, viruses, cosmids and artificial chromosomes. In general, engineered vectors comprise an origin of replication, a multicloning site and a selectable marker. The vector itself is generally a nucleotide sequence, commonly a DNA sequence that comprises an insert (transgene) and a larger sequence that serves as the "backbone" of the vector. Modern vectors may encompass additional features besides the transgene insert and a backbone: promoter, genetic marker, antibiotic resistance, reporter gene, targeting sequence, protein purification tag. Vectors called expression vectors (expression constructs) specifically are for the expression of the transgene in the target cell, and generally have control sequences such as a promoter sequence that drives expression of the transgene. Insertion of a vector into the target cell is usually called "transformation" for bacteria, "transfection" for eukaryotic cells, although insertion of a viral vector is also called "transduction".

As used herein, the term "host cell" is intended to refer to a cell into which a nucleic acid encoding the CD33 targeting compound described herein is introduced by way of transformation, transfection and the like. It should be understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation

or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

As used herein, the term "expression" includes any step involved in the production of a CD33 targeting compound described herein including, but not limited to, transcription, post-transcriptional modification, translation, post-translational modification, and secretion.

The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

A nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice.

The terms "host cell," "target cell" or "recipient cell" are intended to include any individual cell or cell culture that can be or has/have been recipients for vectors or the incorporation of exogenous nucleic acid molecules, polynucleotides and/or proteins. It also is intended to include progeny of a single cell, and the progeny may not necessarily be completely identical (in morphology or in genomic or total DNA complement) to the original parent cell due to natural, accidental, or deliberate mutation. The cells may be prokaryotic or eukaryotic, and include but are not limited to bacteria, yeast cells, animal cells, and mammalian cells, e.g., murine, rat, macaque or human.

Suitable eukaryotic host cells include yeasts, fungi, insect cells and mammalian cells.

The CD33 targeting compound described herein can be produced in bacteria. After expression, the CD33 targeting compound, preferably the antibody construct is isolated from the *E. coli* cell paste in a soluble fraction and can be purified through, e.g., affinity chromatography and/or size exclusion. Final purification can be carried out similar to the process for purifying antibody expressed e. g, in CHO cells.

In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for the CD33 targeting compound described herein. *Saccharomyces cerevisiae*, or common baker's yeast, is the most commonly used among lower eukaryotic host microorganisms. However, a number of other genera, species, and strains are commonly available and useful herein, such as *Schizosaccharomyces pombe*, Kluyveromyces hosts such as, e.g., *K. lactis*, *K. fragilis* (ATCC 12424), *K. bulgaricus* (ATCC 16045), *K. wickerhamii* (ATCC 24178), *K. waltii* (ATCC 56500), *K. drosophilarum* (ATCC 36906), *K. thermotolerans*, and *K. marxianus*; yarrowia (EP 402 226); *Pichia pastoris* (EP 183 070); *Candida*; *Trichoderma reesia* (EP 244 234); *Neurospora crassa*; Schwanniomyces such as *Schwanniomyces occidentalis*; and filamentous fungi such as, e.g., *Neurospora*, *Penicillium*, *Tolypocladium*, and *Aspergillus* hosts such as *A. nidulans* and *A. niger*.

Suitable host cells for the expression of glycosylated CD33 targeting compounds described herein, preferably antibody derived antibody constructs are derived from multicellular organisms. Examples of invertebrate cells include plant and insect cells. Numerous baculoviral strains and variants and corresponding permissive insect host cells from hosts such as *Spodoptera frugiperda* (caterpillar), *Aedes aegypti* (mosquito), *Aedes albopictus* (mosquito), *Drosophila melanogaster* (fruit fly), and *Bombyx mori* have been identified. A variety of viral strains for transfection are publicly available, e. g. , the L-1 variant of *Autographa californica* NPV and the Bm-5 strain of *Bombyx mori* NPV, and such viruses may be used as the virus herein according to the present invention, particularly for transfection of *Spodoptera frugiperda* cells.

Plant cell cultures of cotton, corn, potato, soybean, petunia, tomato, Arabidopsis and tobacco can also be utilized as hosts. Cloning and expression vectors useful in the production of proteins in plant cell culture are known to those of skill in the art. See e.g. Hiatt *et al.*, Nature (1989) 342: 76-78, Owen *et al.* (1992) Bio/Technology 10: 790-794, Artsaenko *et al.* (1995) The Plant J 8: 745-750, and Fecker *et al.* (1996) Plant Mol Biol 32: 979-986.

However, interest has been greatest in vertebrate cells, and propagation of vertebrate cells in culture (tissue culture) has become a routine procedure. Examples of useful mammalian host cell lines are monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham *et al.* , J. Gen Virol. 36 : 59 (1977)); baby hamster kidney cells (BHK, ATCC CCL 10); Chinese hamster ovary cells/-DHFR (CHO, Urlaub *et al.* , Proc. Natl. Acad. Sci. USA 77: 4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod. 23: 243-251 (1980)); monkey kidney cells (CV1 ATCC CCL 70); African green monkey kidney cells (VERO-76, ATCC CRL1587) ; human cervical carcinoma cells (HELA, ATCC CCL 2); canine kidney cells (MDCK, ATCC CCL 34); buffalo rat liver cells (BRL 3A, ATCC CRL 1442); human lung cells

(W138, ATCC CCL 75); human liver cells (Hep G2, 1413 8065); mouse mammary tumor (MMT 060562, ATCC CCL5 1); TRI cells (Mather *et al.*, Annals N. Y Acad. Sci. 383 : 44-68 (1982)) ; MRC 5 cells; FS4 cells; and a human hepatoma line (Hep G2).

When using recombinant techniques, the CD33 targeting compound described herein can be produced intracellularly, in the periplasmic space, or directly secreted into the medium. If the antibody construct is produced intracellularly, as a first step, the particulate debris, either host cells or lysed fragments, are removed, for example, by centrifugation or ultrafiltration. Carter *et al.*, Bio/Technology 10: 163-167 (1992) describe a procedure for isolating antibodies which are secreted to the periplasmic space of *E. coli*. Briefly, cell paste is thawed in the presence of sodium acetate (pH 3.5), EDTA, and phenylmethylsulfonylfluoride (PMSF) over about 30 min. Cell debris can be removed by centrifugation. Where the antibody is secreted into the medium, supernatants from such expression systems are generally first concentrated using a commercially available protein concentration filter, for example, an Amicon or Millipore Pellicon ultrafiltration unit. A protease inhibitor such as PMSF may be included in any of the foregoing steps to inhibit proteolysis and antibiotics may be included to prevent the growth of adventitious contaminants.

The CD33 targeting compound described herein prepared from the host cells can be purified using, for example, hydroxylapatite chromatography, gel electrophoresis, dialysis, and affinity chromatography, with affinity chromatography being the preferred purification technique.

The matrix to which the affinity ligand is attached is most often agarose, but other matrices are available. Mechanically stable matrices such as controlled pore glass or poly(styrene-divinyl) benzene allow for faster flow rates and shorter processing times than can be achieved with agarose. Where the CD33 targeting compound described herein comprises a CH3 domain, the Bakerbond ABXMresin (J. T. Baker, Phillipsburg, NJ) is useful for purification. Other techniques for protein purification such as fractionation on an ion-exchange column, ethanol precipitation, Reverse Phase HPLC, chromatography on silica, chromatography on heparin SEPHAROSETM chromatography on an anion or cation exchange resin (such as a polyaspartic acid column), chromato-focusing, SDS-PAGE, and ammonium sulfate precipitation are also available depending on the antibody to be recovered.

The term "culturing" refers to the in vitro maintenance, differentiation, growth, proliferation and/or propagation of cells under suitable conditions in a medium.

As used herein, the term "pharmaceutical composition" relates to a composition for administration to a patient, preferably a human patient. The particular preferred

pharmaceutical composition of this invention comprises a CD33 targeting compound and at least one epigenetic factor, either in one single formulation or in separate formulations. Preferably, the pharmaceutical composition comprises suitable formulations of carriers, stabilizers and/or excipients. In a preferred embodiment, the pharmaceutical composition comprises a composition for parenteral, transdermal, intraluminal, intraarterial, intrathecal and/or intranasal administration or by direct injection into tissue. It is in particular envisaged that said composition is administered to a patient via infusion or injection. Administration of the suitable compositions may be effected by different ways, e.g., by intravenous, intraperitoneal, subcutaneous, intramuscular, topical or intradermal administration. In particular, the present invention provides for an uninterrupted administration of the suitable composition. As a non-limiting example, uninterrupted, i.e. continuous administration may be realized by a small pump system worn by the patient for metering the influx of therapeutic agent into the body of the patient. The pharmaceutical composition comprising the CD33 targeting compound or the CD33 targeting compound and at least one epigenetic factor can be administered by using said pump systems. Such pump systems are generally known in the art, and commonly rely on periodic exchange of cartridges containing the therapeutic agent to be infused. When exchanging the cartridge in such a pump system, a temporary interruption of the otherwise uninterrupted flow of therapeutic agent into the body of the patient may ensue. In such a case, the phase of administration prior to cartridge replacement and the phase of administration following cartridge replacement would still be considered within the meaning of the pharmaceutical means and methods of the invention together make up one "uninterrupted administration" of such therapeutic agent.

The continuous or uninterrupted administration of the CD33 targeting compound described herein or the CD33 targeting compound and at least one epigenetic factor described herein may be intravenous or subcutaneous by way of a fluid delivery device or small pump system including a fluid driving mechanism for driving fluid out of a reservoir and an actuating mechanism for actuating the driving mechanism. Pump systems for subcutaneous administration may include a needle or a cannula for penetrating the skin of a patient and delivering the suitable composition into the patient's body. Said pump systems may be directly fixed or attached to the skin of the patient independently of a vein, artery or blood vessel, thereby allowing a direct contact between the pump system and the skin of the patient. The pump system can be attached to the skin of the patient for 24 hours up to several days. The pump system may be of small size with a reservoir for small volumes. As a non-limiting example, the volume of the reservoir for the suitable pharmaceutical composition to be administered can be between 0.1 and 50 ml.

The continuous administration may be transdermal by way of a patch worn on the skin and replaced at intervals. One of skill in the art is aware of patch systems for drug delivery suitable for this purpose. It is of note that transdermal administration is especially amenable to uninterrupted administration, as exchange of a first exhausted patch can advantageously be accomplished simultaneously with the placement of a new, second patch, for example on the surface of the skin immediately adjacent to the first exhausted patch and immediately prior to removal of the first exhausted patch. Issues of flow interruption or power cell failure do not arise.

The inventive compositions may further comprise a pharmaceutically acceptable carrier.

Examples of suitable pharmaceutical carriers are well known in the art and include solutions, e.g. phosphate buffered saline solutions, water, emulsions, such as oil/water emulsions, various types of wetting agents, sterile solutions, liposomes, etc. Compositions comprising such carriers can be formulated by well known conventional methods. Formulations can comprise carbohydrates, buffer solutions, amino acids and/or surfactants. Carbohydrates may be non-reducing sugars, preferably trehalose, sucrose, octasulfate, sorbitol or xylitol. In general, as used herein, "pharmaceutically acceptable carrier" means any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active substances is well known in the art. Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed and include: additional buffering agents; preservatives; co-solvents; antioxidants, including ascorbic acid and methionine; chelating agents such as EDTA; metal complexes (e.g., Zn-protein complexes); biodegradable polymers, such as polyesters; salt-forming counter-ions, such as sodium, polyhydric sugar alcohols; amino acids, such as alanine, glycine, asparagine, 2-phenylalanine, and threonine; sugars or sugar alcohols, such as trehalose, sucrose, octasulfate, sorbitol or xylitol, stachyose, mannose, sorbose, xylose, ribose, myoinositol, galactose, lactitol, ribitol, myoinositol, galactitol, glycerol, cyclitols (e.g., inositol), polyethylene glycol; sulfur containing reducing agents, such as glutathione, thiocetic acid, sodium thioglycolate, thioglycerol, [alpha]-monothioglycerol, and sodium thio sulfate; low molecular weight proteins, such as human serum albumin, bovine serum albumin, gelatin, or other immunoglobulins; and hydrophilic polymers, such as polyvinylpyrrolidone. Such formulations may be used for continuous administrations which may be intravenous or subcutaneous with and/or without pump systems. Amino acids may be charged amino acids, preferably lysine, lysine acetate, arginine, glutamate and/or histidine. Surfactants may be detergents, preferably with a molecular weight of >1.2 KD and/or a polyether, preferably with a molecular weight of >3 KD. Non-limiting examples for preferred detergents are Tween

20, Tween 40, Tween 60, Tween 80 or Tween 85. Non-limiting examples for preferred polyethers are PEG 3000, PEG 3350, PEG 4000 or PEG 5000. Buffer systems used in the present invention can have a preferred pH of 5-9 and may comprise citrate, succinate, phosphate, histidine and acetate.

5 The compositions of the present invention comprising the CD33 targeting compound and at least one epigenetic factor in a single or separate formulations can be administered to the subject at a suitable dose which can be determined e.g. by dose escalating studies by administration of increasing doses of the polypeptide described herein exhibiting cross-species specificity described herein to non-chimpanzee primates, for instance macaques. As
10 set forth above, the CD33 targeting composition described herein exhibiting cross-species specificity described herein can be advantageously used in identical form in preclinical testing in non-chimpanzee primates and as drug in humans. The composition or these compositions can also be administered in combination with additional other proteinaceous and non-proteinaceous drugs. These drugs may be administered simultaneously with the
15 composition comprising the polypeptide described herein as defined herein or separately before or after administration of said polypeptide in timely defined intervals and doses. The dosage regimen will be determined by the attending physician and clinical factors. As is well known in the medical arts, dosages for any one patient depend upon many factors, including the patient's size, body surface area, age, the particular compound to be administered, sex,
20 time and route of administration, general health, and other drugs being administered concurrently.

Preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as
25 ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's, or fixed oils. Intravenous vehicles include fluid and nutrient replenishers, electrolyte replenishers (such as those based on Ringer's dextrose), and the like. Preservatives and other additives
30 may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, inert gases and the like. In addition, the composition of the present invention might comprise proteinaceous carriers, like, e.g., serum albumin or immunoglobulin, preferably of human origin. It is envisaged that the composition of the invention might comprise, in addition to the polypeptide described herein defined herein, further biologically active agents, depending on
35 the intended use of the composition. Such agents might be drugs acting on the gastrointestinal system, drugs acting as cytostatica, drugs preventing hyperuricemia, drugs

inhibiting immunoreactions (e.g. corticosteroids), drugs modulating the inflammatory response, drugs acting on the circulatory system and/or agents such as cytokines known in the art. It is also envisaged that the composition of the present invention comprising the CD33 targeting compound and at least one epigenetic factor in a single or separate formulations is applied in an additional co-therapy, i.e., in combination with another anti-cancer medicament.

The biological activity of the pharmaceutical composition defined herein can be determined for instance by cytotoxicity assays, as described in the following examples, in WO 99/54440 or by Schlereth *et al.* (Cancer Immunol. Immunother. 20 (2005), 1-12). "Efficacy" or "*in vivo* efficacy" as used herein refers to the response to therapy by the pharmaceutical composition of the invention, using e.g. standardized NCI response criteria. The success or *in vivo* efficacy of the therapy using a pharmaceutical composition of the invention refers to the effectiveness of the composition for its intended purpose, i.e. the ability of the composition to cause its desired effect, i.e. depletion of pathologic cells, e.g. tumor cells. The *in vivo* efficacy may be monitored by established standard methods for the respective disease entities including, but not limited to white blood cell counts, differentials, Fluorescence Activated Cell Sorting, bone marrow aspiration. In addition, various disease specific clinical chemistry parameters and other established standard methods may be used. Furthermore, computer-aided tomography, X-ray, nuclear magnetic resonance tomography (e.g. for National Cancer Institute-criteria based response assessment [Cheson BD, Horning SJ, Coiffier B, Shipp MA, Fisher RI, Connors JM, Lister TA, Vose J, Grillo-Lopez A, Hagenbeek A, Cabanillas F, Klippensten D, Hiddemann W, Castellino R, Harris NL, Armitage JO, Carter W, Hoppe R, Canellos GP. Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas. NCI Sponsored International Working Group. J Clin Oncol. 1999 Apr;17(4):1244]), positron-emission tomography scanning, white blood cell counts, differentials, Fluorescence Activated Cell Sorting, bone marrow aspiration, lymph node biopsies/histologies, and various lymphoma specific clinical chemistry parameters (e.g. lactate dehydrogenase) and other established standard methods may be used.

Another major challenge in the development of drugs such as the pharmaceutical composition of the invention is the predictable modulation of pharmacokinetic properties. To this end, a pharmacokinetic profile of the drug candidate, i.e. a profile of the pharmacokinetic parameters that affect the ability of a particular drug to treat a given condition, can be established. Pharmacokinetic parameters of the drug influencing the ability of a drug for treating a certain disease entity include, but are not limited to: half-life, volume of distribution, hepatic first-pass metabolism and the degree of blood serum binding. The efficacy of a given drug agent can be influenced by each of the parameters mentioned above.

"Half-life" means the time where 50% of an administered drug are eliminated through biological processes, e.g. metabolism, excretion, etc.

By "hepatic first-pass metabolism" is meant the propensity of a drug to be metabolized upon first contact with the liver, i.e. during its first pass through the liver.

- 5 "Volume of distribution" means the degree of retention of a drug throughout the various compartments of the body, like e.g. intracellular and extracellular spaces, tissues and organs, etc. and the distribution of the drug within these compartments.

10 "Degree of blood serum binding" means the propensity of a drug to interact with and bind to blood serum proteins, such as albumin, leading to a reduction or loss of biological activity of the drug.

Pharmacokinetic parameters also include bioavailability, lag time (T_{lag}), T_{max}, absorption rates, more onset and/or C_{max} for a given amount of drug administered. "Bioavailability" means the amount of a drug in the blood compartment. "Lag time" means the time delay between the administration of the drug and its detection and measurability in blood or plasma.

15 "T_{max}" is the time after which maximal blood concentration of the drug is reached, and "C_{max}" is the blood concentration maximally obtained with a given drug. The time to reach a blood or tissue concentration of the drug which is required for its biological effect is influenced by all parameters. Pharmacokinetic parameters of comprising a CD33 targeting compound such as a bispecific single chain antibody exhibiting cross-species specificity, which may be determined in preclinical animal testing in non-chimpanzee primates as outlined above, are also set forth e.g. in the publication by Schlereth *et al.* (Cancer Immunol. Immunother. 20 (2005), 1-12).

25 The term "toxicity" as used herein refers to the toxic effects of a drug manifested in adverse events or severe adverse events. These side events might refer to a lack of tolerability of the drug in general and/or a lack of local tolerance after administration. Toxicity could also include teratogenic or carcinogenic effects caused by the drug.

30 The term "safety", "*in vivo* safety" or "tolerability" as used herein defines the administration of a drug without inducing severe adverse events directly after administration (local tolerance) and during a longer period of application of the drug. "Safety", "*in vivo* safety" or "tolerability" can be evaluated e.g. at regular intervals during the treatment and follow-up period. Measurements include clinical evaluation, e.g. organ manifestations, and screening of laboratory abnormalities. Clinical evaluation may be carried out and deviations to normal findings recorded/coded according to NCI-CTC and/or MedDRA standards. Organ

manifestations may include criteria such as allergy/immunology, blood/bone marrow, cardiac arrhythmia, coagulation and the like, as set forth e.g. in the Common Terminology Criteria for adverse events v3.0 (CTCAE). Laboratory parameters which may be tested include for instance hematology, clinical chemistry, coagulation profile and urine analysis and examination of other body fluids such as serum, plasma, lymphoid or spinal fluid, liquor and the like. Safety can thus be assessed e.g. by physical examination, imaging techniques (i.e. ultrasound, x-ray, CT scans, Magnetic Resonance Imaging (MRI), other measures with technical devices (i.e. electrocardiogram), vital signs, by measuring laboratory parameters and recording adverse events. For example, adverse events in non-chimpanzee primates in the uses and methods according to the invention may be examined by histopathological and/or histochemical methods.

The term "effective dose" or "effective dosage" is defined as an amount sufficient to achieve or at least partially achieve the desired effect. The term "therapeutically effective dose" is defined as an amount sufficient to cure or at least partially arrest the disease and its complications in a patient already suffering from the disease. Amounts effective for this use will depend upon the severity of the infection and the general state of the subject's own immune system. The term "patient" includes human and other mammalian subjects that receive either prophylactic or therapeutic treatment.

The term "effective and non-toxic dose" as used herein refers to a tolerable dose of a pharmaceutical composition (i.e. a pharmaceutical composition comprising the CD33 targeting compound and at least one epigenetic factor in a single or separate formulations) which is high enough to cause depletion of pathologic cells, tumor elimination, tumor shrinkage or stabilization of disease without or essentially without major toxic effects. Such effective and non-toxic doses may be determined e.g. by dose escalation studies described in the art and should be below the dose inducing severe adverse side events (dose limiting toxicity, DLT).

The above terms are also referred to e.g. in the Preclinical safety evaluation of biotechnology-derived pharmaceuticals S6; ICH Harmonised Tripartite Guideline; ICH Steering Committee meeting on July 16, 1997.

The appropriate dosage, or therapeutically effective amount, of a pharmaceutical composition comprising the CD33 targeting compound and at least one epigenetic factor in a single or separate formulations will depend on the condition to be treated, the severity of the condition, prior therapy, and the patient's clinical history and response to the therapeutic agent. The proper dose can be adjusted according to the judgment of the attending physician such that it can be administered to the patient one time or over a series of

administrations. The pharmaceutical composition can be administered as a sole therapeutic or in combination with additional therapies such as anti-cancer therapies as needed.

The pharmaceutical compositions of this invention are particularly useful for parenteral administration, i.e., subcutaneously, intramuscularly, intravenously, intra-articular and/or intra-synovial. Parenteral administration can be by bolus injection or continuous infusion.

If the pharmaceutical composition has been lyophilized, the lyophilized material is first reconstituted in an appropriate liquid prior to administration. The lyophilized material may be reconstituted in, e.g., bacteriostatic water for injection (BWFI), physiological saline, phosphate buffered saline (PBS), or the same formulation the protein had been in prior to lyophilization.

It has been surprisingly found in connection with the present invention that specific groups of epigenetic factors relate to an increase of the potency of a therapy approach making use of the engagement of T cells to CD33 positive target cells. 5-azacytidine (Vidaza™) and 5-aza-2'-deoxycytidine (decitabine, Dacogen™) are nucleoside analogs that belong to a class of epigenetic therapeutics and are known to be capable of inducing tumor cell killing through the disruption of protein synthesis and inhibition of DNA methylation. Co-therapy approaches using the CD33 specific antibody lintuzumab and 5-azacytidine lead to an improved lintuzumab-mediated ADCC against AML target cells. However, in such study the incubation of AML cells or macrophages did not affect the CD33 expression on those cells (Sutherland et al. MAb. 2010 Jul-Aug; 2(4): 440–448). Accordingly it has been concluded that since for the mode-of-action of lintuzumab requires a functional interaction between the F_C domain of lintuzumab and the F_Cγ receptor of immune effector cells is required the pretreatment with epigenetic compounds increases the specific phagocytosis of target cells by the effector cells.

Thus the present finding are especially in the light of those known effect surprisingly, since the mode-of-action underlying the target cells lysis by T cells when engaged by the CD33 targeting compounds described herein is completely independent of any F_C-F_Cγ receptor interaction. In contrast to the previous studies, an increase of CD33 surface expression by treatment of target cells with epigenetic factors described herein was observed. Also, as apparent from the mode-of-action underlying the target cells lysis by T cells the observed synergistic effect is independent of any signal-transduction-effect which might be triggered by antibody binding to the CD33 surface molecule (e.g. a signaling pathway involving SHP-1, Syk, or both).

Moreover, as the speed and extent of myeloid leukemia cell blast lysis at a given time point was proportional to CD33 expression, this finding supports that the combination of an

epigenetic therapy and a CD33 directed T cell engager would be synergistically more effective than either therapy administered separately. Accordingly, the described administration of one or more CD33 targeting compound in combination with epigenetic factors described herein may allow for lower doses of a bispecific T cell engager to be effective at a given time point.

As described above, examples for epigenetic factors suitable in the combination therapy approach according to the invention are selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors, hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone demethylase inhibitors and ATRA (All Trans-retinoic acid). The redirected lysis of target cells via the recruitment of T cells by a multispecific, at least bispecific, construct involves cytolytic synapse formation and delivery of perforin and granzymes. The engaged T cells are capable of serial target cell lysis, and are not affected by immune escape mechanisms interfering with peptide antigen processing and presentation, or clonal T cell differentiation; see, for example, WO 2007/042261.

The cytotoxic activity mediated by CD33/CD3 bispecific compounds described herein such as bispecific antibody constructs is preferably measured in a cell-based cytotoxicity assay. It is represented by the EC_{50} value, which corresponds to the half maximal effective concentration (concentration of the compound which induces a cytotoxic response halfway between the baseline and maximum). Preferably, the EC_{50} value of the CD33/CD3 bispecific antibody constructs is $\leq 20,000$ pg/ml, more preferably ≤ 5000 pg/ml, even more preferably ≤ 1000 pg/ml, even more preferably ≤ 500 pg/ml, even more preferably ≤ 350 pg/ml, even more preferably ≤ 320 pg/ml, even more preferably ≤ 250 pg/ml, even more preferably ≤ 100 pg/ml, even more preferably ≤ 50 pg/ml, even more preferably ≤ 10 pg/ml, and most preferably ≤ 5 pg/ml.

Any of the above given EC_{50} values can be combined with any one of the indicated scenarios of a cell-based cytotoxicity assay. For example, when (human) CD8 positive T cells or a macaque T cell line are used as effector cells, the EC_{50} value of the CD33/CD3 bispecific antibody construct is preferably ≤ 1000 pg/ml, more preferably ≤ 500 pg/ml, even more preferably ≤ 250 pg/ml, even more preferably ≤ 100 pg/ml, even more preferably ≤ 50 pg/ml, even more preferably ≤ 10 pg/ml, and most preferably ≤ 5 pg/ml. If in this assay the target cells are (human or macaque) CD33 transfected cells such as CHO cells, the EC_{50} value of the CD33/CD3 bispecific antibody construct is preferably ≤ 150 pg/ml, more preferably ≤ 100 pg/ml, even more preferably ≤ 50 pg/ml, even more preferably ≤ 30 pg/ml, even more preferably ≤ 10 pg/ml, and most preferably ≤ 5 pg/ml.

If the target cells are a CD33 positive natural expresser cell line, then the EC₅₀ value is preferably ≤350 pg/ml, more preferably ≤320 pg/ml, even more preferably ≤250 pg/ml, even more preferably ≤200 pg/ml, even more preferably ≤100 pg/ml, even more preferably ≤150 pg/ml, even more preferably ≤100 pg/ml, and most preferably ≤50 pg/ml, or lower.

- 5 When (human) PBMCs are used as effector cells, the EC₅₀ value of the CD33/CD3 bispecific antibody construct is preferably ≤1000 pg/ml, more preferably ≤750 pg/ml, more preferably ≤500 pg/ml, even more preferably ≤350 pg/ml, even more preferably ≤320 pg/ml, even more preferably ≤250 pg/ml, even more preferably ≤100 pg/ml, and most preferably ≤50 pg/ml, or lower.
- 10 The difference in cytotoxic activity between the monomeric and the dimeric isoform of individual CD33/CD3 bispecific antibody constructs is referred to as “potency gap”. This potency gap can e.g. be calculated as ratio between EC₅₀ values of the molecule’s monomeric and dimeric form. Potency gaps of the CD33/CD3 bispecific antibody constructs described herein are preferably ≤5, more preferably ≤4, even more preferably ≤3, even more
15 preferably ≤2 and most preferably ≤1.

It is particularly preferred for the CD33 targeting compound described herein that the second binding domain capable of binding to the T cell CD3 receptor complex comprises a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from:

- (a) CDR-L1 as depicted in SEQ ID NO: 27 of WO 2008/119567, CDR-L2 as depicted in
20 SEQ ID NO: 28 of WO 2008/119567 and CDR-L3 as depicted in SEQ ID NO: 29 of WO 2008/119567;
- (b) CDR-L1 as depicted in SEQ ID NO: 117 of WO 2008/119567, CDR-L2 as depicted in SEQ ID NO: 118 of WO 2008/119567 and CDR-L3 as depicted in SEQ ID NO: 119 of WO 2008/119567; and
- 25 (c) CDR-L1 as depicted in SEQ ID NO: 153 of WO 2008/119567, CDR-L2 as depicted in SEQ ID NO: 154 of WO 2008/119567 and CDR-L3 as depicted in SEQ ID NO: 155 of WO 2008/119567.

- In an alternatively preferred embodiment of the CD33 targeting compound described herein, the second binding domain capable of binding to the T cell CD3 receptor complex comprises
30 a VH region comprising CDR-H 1, CDR-H2 and CDR-H3 selected from:

- (a) CDR-H1 as depicted in SEQ ID NO: 12 of WO 2008/119567, CDR-H2 as depicted in SEQ ID NO: 13 of WO 2008/119567 and CDR-H3 as depicted in SEQ ID NO: 14 of WO 2008/119567;
- (b) CDR-H1 as depicted in SEQ ID NO: 30 of WO 2008/119567, CDR-H2 as depicted in
35 SEQ ID NO: 31 of WO 2008/119567 and CDR-H3 as depicted in SEQ ID NO: 32 of WO 2008/119567;

(c) CDR-H1 as depicted in SEQ ID NO: 48 of WO 2008/119567, CDR-H2 as depicted in SEQ ID NO: 49 of WO 2008/119567 and CDR-H3 as depicted in SEQ ID NO: 50 of WO 2008/119567;

(d) CDR-H1 as depicted in SEQ ID NO: 66 of WO 2008/119567, CDR-H2 as depicted in SEQ ID NO: 67 of WO 2008/119567 and CDR-H3 as depicted in SEQ ID NO: 68 of WO 2008/119567;

(e) CDR-H1 as depicted in SEQ ID NO: 84 of WO 2008/119567, CDR-H2 as depicted in SEQ ID NO: 85 of WO 2008/119567 and CDR-H3 as depicted in SEQ ID NO: 86 of WO 2008/119567;

(f) CDR-H1 as depicted in SEQ ID NO: 102 of WO 2008/119567, CDR-H2 as depicted in SEQ ID NO: 103 of WO 2008/119567 and CDR-H3 as depicted in SEQ ID NO: 104 of WO 2008/119567;

(g) CDR-H1 as depicted in SEQ ID NO: 120 of WO 2008/119567, CDR-H2 as depicted in SEQ ID NO: 121 of WO 2008/119567 and CDR-H3 as depicted in SEQ ID NO: 122 of WO 2008/119567;

(h) CDR-H1 as depicted in SEQ ID NO: 138 of WO 2008/119567, CDR-H2 as depicted in SEQ ID NO: 139 of WO 2008/119567 and CDR-H3 as depicted in SEQ ID NO: 140 of WO 2008/119567;

(i) CDR-H1 as depicted in SEQ ID NO: 156 of WO 2008/119567, CDR-H2 as depicted in SEQ ID NO: 157 of WO 2008/119567 and CDR-H3 as depicted in SEQ ID NO: 158 of WO 2008/119567; and

(j) CDR-H1 as depicted in SEQ ID NO: 174 of WO 2008/119567, CDR-H2 as depicted in SEQ ID NO: 175 of WO 2008/119567 and CDR-H3 as depicted in SEQ ID NO: 176 of WO 2008/119567.

It is further preferred for the CD33 targeting compound described herein that the second binding domain capable of binding to the T cell CD3 receptor complex comprises a VL region selected from the group consisting of a VL region as depicted in SEQ ID NO: 35, 39, 125, 129, 161 or 165 of WO 2008/119567.

It is alternatively preferred that the second binding domain capable of binding to the T cell CD3 receptor complex comprises a VH region selected from the group consisting of a VH region as depicted in SEQ ID NO: 15, 19, 33, 37, 51, 55, 69, 73, 87, 91, 105, 109, 123, 127, 141, 145, 159, 163, 177 or 181 of WO 2008/119567.

More preferably, the CD33 targeting compound described herein is characterized by the second binding domain capable of binding to the T cell CD3 receptor complex comprising a VL region and a VH region selected from the group consisting of:

(a) a VL region as depicted in SEQ ID NO: 17 or 21 of WO 2008/119567 and a VH region as depicted in SEQ ID NO: 15 or 19 of WO 2008/119567;

(b) a VL region as depicted in SEQ ID NO: 35 or 39 of WO 2008/119567 and a VH region as depicted in SEQ ID NO: 33 or 37 of WO 2008/119567;

(c) a VL region as depicted in SEQ ID NO: 53 or 57 of WO 2008/119567 and a VH region as depicted in SEQ ID NO: 51 or 55 of WO 2008/119567;

5 (d) a VL region as depicted in SEQ ID NO: 71 or 75 of WO 2008/119567 and a VH region as depicted in SEQ ID NO: 69 or 73 of WO 2008/119567;

(e) a VL region as depicted in SEQ ID NO: 89 or 93 of WO 2008/119567 and a VH region as depicted in SEQ ID NO: 87 or 91 of WO 2008/119567;

10 (f) a VL region as depicted in SEQ ID NO: 107 or 111 of WO 2008/119567 and a VH region as depicted in SEQ ID NO: 105 or 109 of WO 2008/119567;

(g) a VL region as depicted in SEQ ID NO: 125 or 129 of WO 2008/119567 and a VH region as depicted in SEQ ID NO: 123 or 127 of WO 2008/119567;

(h) a VL region as depicted in SEQ ID NO: 143 or 147 of WO 2008/119567 and a VH region as depicted in SEQ ID NO: 141 or 145 of WO 2008/119567;

15 (i) a VL region as depicted in SEQ ID NO: 161 or 165 of WO 2008/119567 and a VH region as depicted in SEQ ID NO: 159 or 163 of WO 2008/119567; and

(j) a VL region as depicted in SEQ ID NO: 179 or 183 of WO 2008/119567 and a VH region as depicted in SEQ ID NO: 177 or 181 of WO 2008/119567.

20 According to a preferred embodiment of the CD33 targeting compound described herein, in particular the second binding domain capable of binding to the T cell CD3 receptor complex, the pairs of VH-regions and VL-regions are in the format of a single chain antibody (scFv). The VH and VL regions are arranged in the order VH-VL or VL-VH. It is preferred that the VH-region is positioned N-terminally to a linker sequence. The VL-region is positioned C-terminally of the linker sequence.

25 A preferred embodiment of the CD33 targeting compound described herein is characterized by the second binding domain capable of binding to the T cell CD3 receptor complex comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 23, 25, 41, 43, 59, 61, 77, 79, 95, 97, 113, 115, 131, 133, 149, 151, 167, 169, 185 or 187 of WO 2008/119567.

30 The formulations described herein are useful as pharmaceutical compositions in the treatment, amelioration and/or prevention of the pathological medical condition as described herein in a patient in need thereof. The term "treatment" refers to both therapeutic treatment and prophylactic or preventative measures. Treatment includes the application or administration of the formulation to the body, an isolated tissue, or cell from a patient who
35 has a disease/disorder, a symptom of a disease/disorder, or a predisposition toward a disease/disorder, with the purpose to cure, heal, alleviate, relieve, alter, remedy, ameliorate,

improve, or affect the disease, the symptom of the disease, or the predisposition toward the disease.

Those "in need of treatment" include those already with the disorder, as well as those in which the disorder is to be prevented. The term "disease" is any condition that would benefit from treatment with the protein formulation described herein. This includes chronic and acute disorders or diseases including those pathological conditions that predispose the mammal to the disease in question. Non-limiting examples of diseases/disorders to be treated herein include the herein described myeloid leukemia.

In some embodiments, the invention provides a pharmaceutical composition comprising a therapeutically effective amount of one or a plurality of the antibody construct described herein together with a pharmaceutically effective diluents, carrier, solubilizer, emulsifier, preservative, and/or adjuvant. Pharmaceutical compositions described herein include, but are not limited to, liquid, frozen, and lyophilized compositions.

Preferably, formulation materials are nontoxic to recipients at the dosages and concentrations employed.

In certain embodiments, the pharmaceutical composition may contain formulation materials for modifying, maintaining or preserving, for example, the pH, osmolarity, viscosity, clarity, color, isotonicity, odor, sterility, stability, rate of dissolution or release, adsorption or penetration of the composition. In such embodiments, suitable formulation materials include, but are not limited to, amino acids (such as glycine, glutamine, asparagine, arginine, proline, or lysine); antimicrobials; antioxidants (such as ascorbic acid, sodium sulfite or sodium hydrogen-sulfite); buffers (such as borate, bicarbonate, Tris-HCl, citrates, phosphates or other organic acids); bulking agents (such as mannitol or glycine); chelating agents (such as ethylenediamine tetraacetic acid (EDTA)); complexing agents (such as caffeine, polyvinylpyrrolidone, beta-cyclodextrin or hydroxypropyl-beta-cyclodextrin); fillers; monosaccharides; disaccharides; and other carbohydrates (such as glucose, mannose or dextrans); proteins (such as serum albumin, gelatin or immunoglobulins); coloring, flavoring and diluting agents; emulsifying agents; hydrophilic polymers (such as polyvinylpyrrolidone); low molecular weight polypeptides; salt-forming counterions (such as sodium); preservatives (such as benzalkonium chloride, benzoic acid, salicylic acid, thimerosal, phenethyl alcohol, methylparaben, propylparaben, chlorhexidine, sorbic acid or hydrogen peroxide); solvents (such as glycerin, propylene glycol or polyethylene glycol); sugar alcohols (such as mannitol or sorbitol); suspending agents; surfactants or wetting agents (such as pluronics, PEG, sorbitan esters, polysorbates such as polysorbate 20, polysorbate, triton, tromethamine, lecithin, cholesterol, tyloxapal); stability enhancing agents (such as sucrose or sorbitol);

tonicity enhancing agents (such as alkali metal halides, preferably sodium or potassium chloride, mannitol sorbitol); delivery vehicles; diluents; excipients and/or pharmaceutical adjuvants. See, REMINGTON'S PHARMACEUTICAL SCIENCES, 18th Edition, (A. R. Genmo, ed.), 1990, Mack Publishing Company.

- 5 In certain embodiments, the optimal pharmaceutical composition will be determined by one skilled in the art depending upon, for example, the intended route of administration, delivery format and desired dosage. See, for example, REMINGTON'S PHARMACEUTICAL SCIENCES, *supra*. In certain embodiments, such compositions may influence the physical state, stability, rate of in vivo release and rate of in vivo clearance of the antigen binding
- 10 proteins described herein. In certain embodiments, the primary vehicle or carrier in a pharmaceutical composition may be either aqueous or non-aqueous in nature. For example, a suitable vehicle or carrier may be water for injection, physiological saline solution or artificial cerebrospinal fluid, possibly supplemented with other materials common in compositions for parenteral administration. Neutral buffered saline or saline mixed with
- 15 serum albumin are further exemplary vehicles. In specific embodiments, pharmaceutical compositions comprise Tris buffer of about pH 7.0-8.5, or acetate buffer of about pH 4.0-5.5, and may further include sorbitol or a suitable substitute therefore. In certain embodiments of the invention, human antibody or antigen binding fragment thereof described herein or the antibody construct described herein compositions may be prepared for storage by mixing the
- 20 selected composition having the desired degree of purity with optional formulation agents (REMINGTON'S PHARMACEUTICAL SCIENCES, *supra*) in the form of a lyophilized cake or an aqueous solution. Further, in certain embodiments, the human antibody or antigen binding fragment thereof described herein or the antibody construct described herein may be formulated as a lyophilizate using appropriate excipients such as sucrose.
- 25 The pharmaceutical compositions described herein can be selected for parenteral delivery. Alternatively, the compositions may be selected for inhalation or for delivery through the digestive tract, such as orally. Preparation of such pharmaceutically acceptable compositions is within the skill of the art. The formulation components are present preferably in concentrations that are acceptable to the site of administration. In certain embodiments,
- 30 buffers are used to maintain the composition at physiological pH or at a slightly lower pH, typically within a pH range of from about 5 to about 8.

When parenteral administration is contemplated, the therapeutic compositions for use in this invention may be provided in the form of a pyrogen-free, parenterally acceptable aqueous solution comprising the desired human antibody or antigen binding fragment thereof

35 described herein or the antibody construct described herein in a pharmaceutically acceptable vehicle. A particularly suitable vehicle for parenteral injection is sterile distilled

water in which the antibody construct described herein is formulated as a sterile, isotonic solution, properly preserved. In certain embodiments, the preparation can involve the formulation of the desired molecule with an agent, such as injectable microspheres, bio-erodible particles, polymeric compounds (such as polylactic acid or polyglycolic acid), beads
5 or liposomes, that may provide controlled or sustained release of the product which can be delivered via depot injection. In certain embodiments, hyaluronic acid may also be used, having the effect of promoting sustained duration in the circulation. In certain embodiments, implantable drug delivery devices may be used to introduce the desired antigen binding protein.

10 Additional pharmaceutical compositions will be evident to those skilled in the art, including formulations involving the antibody construct described herein in sustained- or controlled-delivery formulations. Techniques for formulating a variety of other sustained- or controlled-delivery means, such as liposome carriers, bio-erodible microparticles or porous beads and depot injections, are also known to those skilled in the art. See, for example, International
15 Patent Application No. PCT/US93/00829, which is incorporated by reference and describes controlled release of porous polymeric microparticles for delivery of pharmaceutical compositions. Sustained-release preparations may include semipermeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules. Sustained release matrices may include polyesters, hydrogels, polylactides (as disclosed in U.S. Pat. No. 3,773,919 and
20 European Patent Application Publication No. EP 058481, each of which is incorporated by reference), copolymers of L-glutamic acid and gamma ethyl-L-glutamate (Sidman et al., 1983, Biopolymers 2:547-556), poly (2-hydroxyethyl-methacrylate) (Langer et al., 1981, J. Biomed. Mater. Res. 15:167-277 and Langer, 1982, Chem. Tech. 12:98-105), ethylene vinyl acetate (Langer et al., 1981, supra) or poly-D(-)-3-hydroxybutyric acid (European Patent
25 Application Publication No. EP 133,988). Sustained release compositions may also include liposomes that can be prepared by any of several methods known in the art. See, e.g., Eppstein et al., 1985, Proc. Natl. Acad. Sci. U.S.A. 82:3688-3692; European Patent Application Publication Nos. EP 036,676; EP 088,046 and EP 143,949, incorporated by reference.

30 Pharmaceutical compositions used for in vivo administration are typically provided as sterile preparations. Sterilization can be accomplished by filtration through sterile filtration membranes. When the composition is lyophilized, sterilization using this method may be conducted either prior to or following lyophilization and reconstitution. Compositions for parenteral administration can be stored in lyophilized form or in a solution. Parenteral
35 compositions generally are placed into a container having a sterile access port, for example,

an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Aspects of the invention includes self-buffering antibody construct formulations, which can be used as pharmaceutical compositions, as described in international patent application
5 WO 2006/138181A2 (PCT/US2006/022599), which is incorporated by reference in its entirety herein.

As discussed above, certain embodiments involve antibody construct protein compositions, particularly pharmaceutical compositions of the invention, that comprise, in addition to the antibody construct described herein, one or more excipients such as those illustratively
10 described in this section and elsewhere herein. Excipients can be used in the invention in this regard for a wide variety of purposes, such as adjusting physical, chemical, or biological properties of formulations, such as adjustment of viscosity, and or processes to improve effectiveness and or to stabilize such formulations and processes against degradation and spoilage due to, for instance, stresses that occur during manufacturing, shipping, storage,
15 pre-use preparation, administration, and thereafter.

A variety of expositions are available on protein stabilization and formulation materials and methods useful in this regard, such as Arakawa et al., "Solvent interactions in pharmaceutical formulations," Pharm Res. 8(3): 285-91 (1991); Kendrick et al., "Physical stabilization of proteins in aqueous solution," in: RATIONAL DESIGN OF STABLE PROTEIN
20 FORMULATIONS: THEORY AND PRACTICE, Carpenter and Manning, eds. Pharmaceutical Biotechnology. 13: 61-84 (2002), and Randolph et al., "Surfactant-protein interactions," Pharm Biotechnol. 13: 159-75 (2002), each of which is herein incorporated by reference in its entirety, particularly in parts pertinent to excipients and processes of the same for self-buffering protein formulations in accordance with the current invention,
25 especially as to protein pharmaceutical products and processes for veterinary and/or human medical uses.

Salts may be used in accordance with certain embodiments of the invention to, for example, adjust the ionic strength and/or the isotonicity of a formulation and/or to improve the solubility and/or physical stability of a protein or other ingredient of a composition in accordance with
30 the invention.

As is well known, ions can stabilize the native state of proteins by binding to charged residues on the protein's surface and by shielding charged and polar groups in the protein and reducing the strength of their electrostatic interactions, attractive, and repulsive interactions. Ions also can stabilize the denatured state of a protein by binding to, in
35 particular, the denatured peptide linkages (--CONH) of the protein. Furthermore, ionic

interaction with charged and polar groups in a protein also can reduce intermolecular electrostatic interactions and, thereby, prevent or reduce protein aggregation and insolubility.

Ionic species differ significantly in their effects on proteins. A number of categorical rankings of ions and their effects on proteins have been developed that can be used in formulating pharmaceutical compositions in accordance with the invention. One example is the Hofmeister series, which ranks ionic and polar non-ionic solutes by their effect on the conformational stability of proteins in solution. Stabilizing solutes are referred to as "kosmotropic." Destabilizing solutes are referred to as "chaotropic." Kosmotropes commonly are used at high concentrations (e.g., >1 molar ammonium sulfate) to precipitate proteins from solution ("salting-out"). Chaotropes commonly are used to denature and/or to solubilize proteins ("salting-in"). The relative effectiveness of ions to "salt-in" and "salt-out" defines their position in the Hofmeister series.

Free amino acids can be used in the antibody construct formulations in accordance with various embodiments of the invention as bulking agents, stabilizers, and antioxidants, as well as other standard uses. Lysine, proline, serine, and alanine can be used for stabilizing proteins in a formulation. Glycine is useful in lyophilization to ensure correct cake structure and properties. Arginine may be useful to inhibit protein aggregation, in both liquid and lyophilized formulations. Methionine is useful as an antioxidant.

Polyols include sugars, e.g., mannitol, sucrose, and sorbitol and polyhydric alcohols such as, for instance, glycerol and propylene glycol, and, for purposes of discussion herein, polyethylene glycol (PEG) and related substances. Polyols are kosmotropic. They are useful stabilizing agents in both liquid and lyophilized formulations to protect proteins from physical and chemical degradation processes. Polyols also are useful for adjusting the tonicity of formulations.

Among polyols useful in select embodiments of the invention is mannitol, commonly used to ensure structural stability of the cake in lyophilized formulations. It ensures structural stability to the cake. It is generally used with a lyoprotectant, e.g., sucrose. Sorbitol and sucrose are among preferred agents for adjusting tonicity and as stabilizers to protect against freeze-thaw stresses during transport or the preparation of bulks during the manufacturing process.

Reducing sugars (which contain free aldehyde or ketone groups), such as glucose and lactose, can glycate surface lysine and arginine residues. Therefore, they generally are not among preferred polyols for use in accordance with the invention. In addition, sugars that form such reactive species, such as sucrose, which is hydrolyzed to fructose and glucose under acidic conditions, and consequently engenders glycation, also is not among preferred

polyols of the invention in this regard. PEG is useful to stabilize proteins and as a cryoprotectant and can be used in the invention in this regard.

Embodiments of the antibody construct formulations further comprise surfactants. Protein molecules may be susceptible to adsorption on surfaces and to denaturation and consequent aggregation at air-liquid, solid-liquid, and liquid-liquid interfaces. These effects generally scale inversely with protein concentration. These deleterious interactions generally scale inversely with protein concentration and typically are exacerbated by physical agitation, such as that generated during the shipping and handling of a product.

Surfactants routinely are used to prevent, minimize, or reduce surface adsorption. Useful surfactants in the invention in this regard include polysorbate 20, polysorbate 80, other fatty acid esters of sorbitan polyethoxylates, and poloxamer 188.

Surfactants also are commonly used to control protein conformational stability. The use of surfactants in this regard is protein-specific since, any given surfactant typically will stabilize some proteins and destabilize others.

Polysorbates are susceptible to oxidative degradation and often, as supplied, contain sufficient quantities of peroxides to cause oxidation of protein residue side-chains, especially methionine. Consequently, polysorbates should be used carefully, and when used, should be employed at their lowest effective concentration. In this regard, polysorbates exemplify the general rule that excipients should be used in their lowest effective concentrations.

Embodiments of the antibody construct formulations further comprise one or more antioxidants. To some extent deleterious oxidation of proteins can be prevented in pharmaceutical formulations by maintaining proper levels of ambient oxygen and temperature and by avoiding exposure to light. Antioxidant excipients can be used as well to prevent oxidative degradation of proteins. Among useful antioxidants in this regard are reducing agents, oxygen/free-radical scavengers, and chelating agents. Antioxidants for use in therapeutic protein formulations in accordance with the invention preferably are water-soluble and maintain their activity throughout the shelf life of a product. EDTA is a preferred antioxidant in accordance with the invention in this regard.

Antioxidants can damage proteins. For instance, reducing agents, such as glutathione in particular, can disrupt intramolecular disulfide linkages. Thus, antioxidants for use in the invention are selected to, among other things, eliminate or sufficiently reduce the possibility of themselves damaging proteins in the formulation.

Formulations in accordance with the invention may include metal ions that are protein co-factors and that are necessary to form protein coordination complexes, such as zinc

necessary to form certain insulin suspensions. Metal ions also can inhibit some processes that degrade proteins. However, metal ions also catalyze physical and chemical processes that degrade proteins.

Magnesium ions (10-120 mM) can be used to inhibit isomerization of aspartic acid to isoaspartic acid. Ca^{+2} ions (up to 100 mM) can increase the stability of human deoxyribonuclease. Mg^{+2} , Mn^{+2} , and Zn^{+2} , however, can destabilize rhDNase. Similarly, Ca^{+2} and Sr^{+2} can stabilize Factor VIII, it can be destabilized by Mg^{+2} , Mn^{+2} and Zn^{+2} , Cu^{+2} and Fe^{+2} , and its aggregation can be increased by Al^{+3} ions.

Embodiments of the antibody construct formulations further comprise one or more preservatives. Preservatives are necessary when developing multi-dose parenteral formulations that involve more than one extraction from the same container. Their primary function is to inhibit microbial growth and ensure product sterility throughout the shelf-life or term of use of the drug product. Commonly used preservatives include benzyl alcohol, phenol and m-cresol. Although preservatives have a long history of use with small-molecule parenterals, the development of protein formulations that includes preservatives can be challenging. Preservatives almost always have a destabilizing effect (aggregation) on proteins, and this has become a major factor in limiting their use in multi-dose protein formulations. To date, most protein drugs have been formulated for single-use only. However, when multi-dose formulations are possible, they have the added advantage of enabling patient convenience, and increased marketability. A good example is that of human growth hormone (hGH) where the development of preserved formulations has led to commercialization of more convenient, multi-use injection pen presentations. At least four such pen devices containing preserved formulations of hGH are currently available on the market. Norditropin (liquid, Novo Nordisk), Nutropin AQ (liquid, Genentech) & Genotropin (lyophilized--dual chamber cartridge, Pharmacia & Upjohn) contain phenol while Somatropin (Eli Lilly) is formulated with m-cresol. Several aspects need to be considered during the formulation and development of preserved dosage forms. The effective preservative concentration in the drug product must be optimized. This requires testing a given preservative in the dosage form with concentration ranges that confer anti-microbial effectiveness without compromising protein stability.

As might be expected, development of liquid formulations containing preservatives are more challenging than lyophilized formulations. Freeze-dried products can be lyophilized without the preservative and reconstituted with a preservative containing diluent at the time of use. This shortens the time for which a preservative is in contact with the protein, significantly minimizing the associated stability risks. With liquid formulations, preservative effectiveness and stability should be maintained over the entire product shelf-life (about 18 to 24 months).

An important point to note is that preservative effectiveness should be demonstrated in the final formulation containing the active drug and all excipient components.

The antibody construct described herein generally will be designed for specific routes and methods of administration, for specific administration dosages and frequencies of administration, for specific treatments of specific diseases, with ranges of bio-availability and persistence, among other things. Formulations thus may be designed in accordance with the invention for delivery by any suitable route, including but not limited to orally, aurally, ophthalmically, rectally, and vaginally, and by parenteral routes, including intravenous and intraarterial injection, intramuscular injection, and subcutaneous injection.

Once the pharmaceutical composition has been formulated, it may be stored in sterile vials as a solution, suspension, gel, emulsion, solid, crystal, or as a dehydrated or lyophilized powder. Such formulations may be stored either in a ready-to-use form or in a form (e.g., lyophilized) that is reconstituted prior to administration. The invention also provides kits for producing a single-dose administration unit. The kits of the invention may each contain both a first container having a dried protein and a second container having an aqueous formulation. In certain embodiments of this invention, kits containing single and multi-chambered pre-filled syringes (e.g., liquid syringes and lyosyringes) are provided. The therapeutically effective amount of an antibody construct protein-containing pharmaceutical composition to be employed will depend, for example, upon the therapeutic context and objectives. One skilled in the art will appreciate that the appropriate dosage levels for treatment will vary depending, in part, upon the molecule delivered, the indication for which the antibody construct described herein is being used, the route of administration, and the size (body weight, body surface or organ size) and/or condition (the age and general health) of the patient. In certain embodiments, the clinician may titer the dosage and modify the route of administration to obtain the optimal therapeutic effect. A typical dosage may range from about 0.1 µg/kg to up to about 30 mg/kg or more, depending on the factors mentioned above. In specific embodiments, the dosage may range from 1.0 µg/kg up to about 20 mg/kg, optionally from 10 µg/kg up to about 10 mg/kg or from 100 µg/kg up to about 5 mg/kg.

A therapeutic effective amount of pharmaceutical composition of the invention comprising the CD33 targeting compound and at least one epigenetic factor in a single or separate formulations preferably results in a decrease in severity of disease symptoms, in increase in frequency or duration of disease symptom-free periods or a prevention of impairment or disability due to the disease affliction. For treating CD33-expressing tumors, a therapeutically effective amount of the CD33 targeting compound and at least one epigenetic factor in a single or separate formulations, e.g. an anti-CD33/CD3 antibody construct and the

at least one epigenetic factor, preferably inhibits cell growth or tumor growth by at least about 20%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, or at least about 90% relative to untreated patients. The ability of a compounds to inhibit tumor growth may be evaluated in an animal model predictive of efficacy in human tumors.

Pharmaceutical compositions may be administered using a medical device. Examples of medical devices for administering pharmaceutical compositions are described in U.S. Patent Nos. 4,475,196; 4,439,196; 4,447,224; 4,447, 233; 4,486,194; 4,487,603; 4,596,556; 4,790,824; 4,941,880; 5,064,413; 5,312,335; 5,312,335; 5,383,851; and 5,399,163, all incorporated by reference herein.

It should be understood that the inventions herein are not limited to particular methodology, protocols, or reagents, as such can vary. The discussion and examples provided herein are presented for the purpose of describing particular embodiments only and are not intended to limit the scope of the present invention, which is defined solely by the claims.

All publications and patents cited throughout the text of this specification (including all patents, patent applications, scientific publications, manufacturer's specifications, instructions, etc.), whether supra or infra, are hereby incorporated by reference in their entirety. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention. To the extent the material incorporated by reference contradicts or is inconsistent with this specification, the specification will supersede any such material.

Examples:

The following examples are provided for the purpose of illustrating specific embodiments or features of the present invention. These examples should not be construed as to limit the scope of this invention. The examples are included for purposes of illustration, and the present invention is limited only by the claims.

Example 1 – Epigenetic modifying drugs as sensitizing agents for CD33 targeting compound-induced cytotoxicity

The level of CD33 expression was identified as a critical variable for the extent of activity of a CD33 targeting compound described herein such as AMG330 against human AML cells. Accordingly, it was surprising to observe the potential of epigenetic modifying drugs such as histone deacetylase (HDAC) inhibitors or DNA methyltransferase (DNMT) I inhibitors as sensitizing agents for AMG 330-induced cytotoxicity.

For the experimental settings mononuclear cells were collected from healthy adult volunteers via leukapheresis, and T cells enriched through magnetic cell sorting (Pan T Cell Isolation Kit II; Miltenyi Biotec, Auburn, CA). Thawed cell aliquots were labeled with 3 μ M CellVue Burgundy (eBioscience, San Diego, CA) according to the manufacturer's instructions.

- 5 Human myeloid OCI-AML3, KG-1a, ML-1, NB4, TF-1, and HL-60 cells were maintained as previously described (Walter et al. Blood. 2003;102(4):1466-1473; Walter et al. Blood. 2004;103(11):4276-4284, Walter et al. Blood. 2005;105(3):1295-1302).

CD33 expression on parental AML cells and cell lines was quantified by flow cytometry using a phycoerythrin (PE)-conjugated anti-CD33 antibody (clone P67.6; BD Biosciences, San
10 Jose, CA, USA) (see Walter et al. Blood. 2005;105(3):1295-1302).

For the quantification of compound induces cytotoxicity AML cells were taken during exponential growth and incubated at 37°C (in 5% CO₂ and air) in 96-well round bottom plates (BD Falcon™) at 5-10 x 10³ cells/well in 225 μ L culture medium containing various concentrations of AMG 330 as well as T-cells at different effector:target (E:T) cell ratios.
15 After 48 hours, cell numbers and drug-induced cytotoxicity, using 4',6-diamidino-2-phenylindole (DAPI) to detect non-viable cells, were determined using a LSRII flow cytometer (BD Biosciences, San Jose, CA) and analyzed with FlowJo (Tree Star, Ashland, OR). AML cells were identified by forward/side scatter properties and negativity for CellVue Burgundy dye.

20 To determine CD33 modulation, aliquots of AML cells were left untreated or incubated with either AMG 330 (250 pg/mL) or an unconjugated, unlabeled anti-CD33 antibody (clone P67.6; BD Biosciences, San Jose, CA, USA; 2.5 μ g/mL). After 48 hours, cells were washed in ice-cold Phosphate Buffered Saline (PBS, GIBCO Invitrogen) to remove unbound antibody and resuspended in PBS containing 2% fetal bovine serum. As AMG 330 does not compete
25 for binding to CD33 with P67.6, aliquots of untreated and AMG 330-treated cells were incubated with P67.6 or no primary antibody followed by biotin-conjugated rat anti-mouse IgG₁ (used at 2.5 μ g/mL in PBS/2% FBS) and streptavidin-phycoerythrin (PE) (used at 2.5 μ g/mL in PBS/2% FBS: both from BD Biosciences). Likewise, aliquots of untreated and P67.6-treated cells were incubated with unconjugated P67.6 or without primary antibody;
30 cells were then washed and incubated with biotin-conjugated rat anti-mouse IgG₁ monoclonal antibody followed by incubation with streptavidin-PE conjugate. To identify nonviable cells, all samples were stained with DAPI. At least 10,000 events were acquired, and DAPI⁺ cells were analyzed on a Canto flow cytometer (BD Biosciences) using FlowJo Software. Linear median fluorescence intensity (MFI) values were used to calculate the
35 percentage of drug-bound CD33 internalization.

As shown in Figure 1, 3-day pretreatment with the HDAC inhibitor, panobinostat, resulted in significant increase in CD33 expression in OCI-AML3 and, markedly, KG-1a cells. More importantly, relative to untreated cells, cells pretreated with panobinostat for 3 days were modestly more sensitive to AMG 330-induced cytotoxicity (KG-1a > OCI-AML3).

Pretreatment with the DNMT I inhibitor, azacitidine, for 3 days resulted in significant increase in CD33 expression on KG-1a. Consistently, after pretreatment with azacitidine, KG-1a cells became significantly more sensitive to AMG 330-induced cytotoxicity relative to untreated cells (Figure 2).

Example 2 – CD33 up-regulation on AML cells to increase AMG 330 mediated lysis efficacy

Hydroxyurea

Up-regulation of CD33 on AML cell lines:

AML cell lines HL-60, PL21, OCI-AML3, KG1a and MV4-11 were seeded in 24-well plates at 1×10^6 cells/ml on day 0. Cells were either left untreated (UT) or treated with 10 μ M (H1) or 100 μ M (H2) hydroxyurea (Sigma) for three consecutive days (day 0, day 1 and day 2). On day 3, cells were harvested, counted and analyzed for changes in CD33 surface expression level by flow cytometry.

Figure 3 and Table 2 show an upregulation of CD33 on HL-60 and PL21 AML cells in a concentration dependant manner.

CD33 MFI Ratio	UT	H1	H2
HL-60	134.9	171.3	210.0
PL21	166.9	177.9	191.8

Table 2: CD33 MFI Ratios of HL-60 and PL21 AML cells after incubation with/without hydroxyurea determined by flow cytometry.

Up-regulation of CD33 on primary AML cells:

Three primary AML samples were seeded in a 12-well plates at 1×10^6 cells/ml, as previously described (Krupka, Subklewe et.al, Blood 2014). Cells were either left untreated (UT) or treated with 10 μ M (H1) or 100 μ M (H2) hydroxyurea (Sigma) for three consecutive days (day 0, day 1 and day 2). On day 1 - day 3, cells were harvested, counted and analyzed for changes in CD33 surface expression by flow cytometry.

Figure 4 and Table 3 show an up-regulation of CD33 in 1 of 3 patient samples on day 1 and day 2 of incubation with hydroxyurea.

CD33 MFI Ratio	UT	H1	H2
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day 1 Patient 2	3.7	4.2	4.5
day 2 Patient 2	4.8	4.2	5.1

Table 3: CD33 MFI Ratios of primary AML cells from patient 2 after 1 and 2 days of incubation with hydroxyurea determined by flow cytometry.

5 Granulocyte-Colony Stimulating Factor (G-CSF)

Up-regulation of CD33 on AML cell lines:

AML cell lines OCI-AML3 and KG1 α were seeded in 24-well plates at 5×10^5 cells/ml on day 0. Cells were either left untreated (UT) or treated with 200 ng/ml (C1) or 2000 ng/ml (C2) G-CSF (Peprotech) for 10 days. G-CSF was freshly added to the cultures biweekly. On day 10, cells were harvested and analyzed for changes in CD33 surface expression by flow cytometry.

Figure 5 and Table 4 show a low upregulation of CD33 on KG1 α AML cells in an concentration dependant manner.

CD33 MFI Ratio	UT	C1	C2
KG1 α	16.5	17.9	19.2

- 15 Table 4: CD33 MFI Ratios of KG1 α AML cells after 10 days of incubation with/without G-CSF determined by flow cytometry.

SEQ ID NO.	DESIGNATION	SOURCE	TYPE	SEQUENCE
1	CD33 VH of AH3	artificial	aa	QVQLVQSGAEVKKPESVKVSKKASGYTFITNYGMNWRQAPQGQGLEWMGWINTYTGEPITYADDFKG RVTMSDSTSTAYLEINSLRSDDTAIYYCARWSWSDGYVYFDYWGQGT'TVTVSS
2	CD33 HCDR1 of AH3	artificial	aa	NYGMN
3	CD33 HCDR2 of AH3	artificial	aa	WINTYTGEPITYADDFKG
4	CD33 HCDR3 of AH3	artificial	aa	WSWSDGYVYFDY
5	CD33 VH of AH3	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAGGTAAGGCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAACACCTACACTGGAGAGCCAAATATGCTGATGACTTCAAGGGA CGGTTACCATGTCTTCGGATACCTCTACCAGCACTGCCTATTTGGAAATCAACAGCCTCAGAAAT GATGACACGGCTATATATTAATGTGCGCGCTGGAGTTGGAGTGATGTTACTACGTTTACTTTTGAC TACTGGGCAAGGCACTACGGTCACCGTCTCCTCA
6	CD33 VL of AH3	artificial	aa	DIVMTQSPDLSLTSLGERTTINCKSSQSVLDSKKNKNSLAWYQQKPGQPPLKILLSWASTRESGIPD RFSGSGSGTDFTLTIDSLQPEDSATYFCQQSAHFPIITFGQGTTRLEIK
7	CD33 LCDR1 of AH3	artificial	aa	KSSQSVLDSKKNKNSLA
8	CD33 LCDR2 of AH3	artificial	aa	WASTRES
9	CD33 LCDR3 of AH3	artificial	aa	QQSAHFPIIT
10	CD33 VL of AH3	artificial	nt	GACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGACCAACATCAAC TGCAAGTCCAGCCAGAGTGTTTATAGACAGCTCCAAGAAATAAGAACTCCTTAGCTTGGTACCAGCAG AAACCAAGACAGCTCCTAAATTAATCTCTCTCTGGGATCTACGCGGAAATCCGGGATCCCTGAC CGATTCAGTGGCAGCGGCTGGGACAGATTTCACTCTCACTATTTGACAGCCTGCAGCCTGAAGAT TCTGCAACTTACTATTGTCAACAGTCTGCCCACTTCCCGATCACCTTTGGCCAAAGGACACGACTG GAGATTAAA
11	CD33 CD33 HL of AH3	artificial	aa	QVQLVQSGAEVKKPESVKVSKKASGYTFITNYGMNWRQAPQGQGLEWMGWINTYTGEPITYADDFKG RVTMSDSTSTAYLEINSLRSDDTAIYYCARWSWSDGYVYFDYWGQGT'TVTVSSGGGSGGGGS GGGSDIVMTQSPDLSLTSLGERTTINCKSSQSVLDSKKNKNSLAWYQQKPGQPPLKILLSWASTRE SGIPDRFSGSGSGTDFTLTIDSLQPEDSATYFCQQSAHFPIITFGQGTTRLEIK
12	CD33 HL of AH3	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAGGCAAGGCTCCAGGACAGGGT

13	CD33 AH3 HL x H2C HL	artificial	aa	TTAGAGTGGATGGGCTGGATAAAACACCTTACACTGGAGAGCCAAACATATGCTGATGACTTCAAGGGA CGGGTTACCATGTCTTCGGATACCTCTACCAGCACTGCCTATTTGGAAATCAACAGCCTCAGAAAGT GATGACACGGCTATATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGCACTACGGTCAACCGTCTCTCAGGTGGTGGTGGTTCTGGCGGCGGCGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTCTTACAGAGCTCCAAAGAATAAGAACTCCTTA GCTTGGTACCAAGCAAAACAGGACAGCTCCTAAATTTACTCTCTTCTGGCATCTACGCGGAA TCCGGGATCCCTGACCGGATTCAGTGGCAGCGGTCTGGGACAGATTTCACTCTCACTATTGACAGC CTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCATTTCCCGGATCACCTTTGGC CAAGGACACGACTGGAGATTAAA QVQLVQSGAEVKKPESVKVSCKASGYFTNYGMNWNVRQAPGQGLEWMGWINTYTGEPYADDFKG RVTMSDSTSTAYLEINSLRSDDTAIYYCARWSWSDGYVYFDYWGQGTITVTVSSGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSKNKNKSLAWYQQPKPQLLLSWASTRE SGIPDRFSGSGGTDFLTIDSLQPEDSATYYCQQSAHFPITFGQGTREIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAASGFTFNKYAMNWNVRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTITVTVSSGGGSGGGGSGGGGS QTIVTQEPSTLTVSPGGTFTLTTCGSSSTGAVTSGYYPNWQQKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGKAAALTLGVQVPEDEAEFYCALMYSNRWVFGGKLTIVL
14	CD33 AH3 HL x H2C HL	artificial	nt	CAGGTGACAGCTGGTGACGTGGAGCTGAGGTGAAAAAGCCTGGAGAGTCAGTCAAGGTCTCTCTGC AAGGTAGCGGTATACCTTCACAAAATATGGAATGAACTGGGTGAGGACAGGTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCCAAACATATGCTGATGACTTCAAGGGA CGGGTTACCATGTCTTCGGATACCTCTACCAGCACTGCCTATTTGGAAATCAACAGCCTCAGAAAGT GATGACACGGCTATATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGCACTACGGTCAACCGTCTCTCAGGTGGTGGTGGTTCTGGCGGCGGCGCTCC GGTGGTGGTGGTCTTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTCTTACAGAGCTCCAAAGAATAAGAACTCCTTA GCTTGGTACCAAGCAAAACAGGACAGCTCCTAAATTTACTCTCTTCTGGCATCTACGCGGAA TCCGGGATCCCTGACCGGATTCAGTGGCAGCGGTCTGGGACAGATTTCACTCTCACTATTGACAGC CTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCATTTCCCGGATCACCTTTGGC CAAGGACACGACTGGAGATTAAAATCCGAGGTGGTGGTCCGAGGTGAGTGGTCGAGTCTGGA GGAGGATGGGTGACGCTGGAGGGTTCATGAAACTCTCATGTGCAGCCTCTGGATTCACCTTCAAT AAGTACGCCATGAACTGGGTCCGCCAGGTCCAGGAAAGGGTTTGGAAATGGGTTCGTCGCATAAGA AGTAAAATAATAATAATAATGCAACATATATGCGCATTCAGTGAAGACAGGTTACCATCTCCAGA GATGATTCAAAAAACACCTGCCATCTACAAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAAATAGCTACATATCTTACTGGGTCTACTGGGGCCAAAGG ACTCTGGTCAACCGTCTCTCAGGTGGTGGTGGTCTTGGCGGCGGCGGTCCGGTGGTGGTGGTCT CAGACTGTGTGTGACTCAGGAACCTTCACCTACCGGTATCACCTGGTGAACAGTCACTCACTTGT GGCTCCTCGACTGGGGCTGTATACATCTGGCTACTACCCAAACTGGGTCCACAAAAACAGGTCTAG GCACCCCGTGGTCTAATAGGTGGGACTAAGTTCTCTCGCCCCGGTACTCTCTGCCAGATTCTCAGGC

15	CD33 AH3 HL x F12Q HL	artificial	aa	TCCCTGCTTGGAGGCAAGGCTGCCCTCACCCCTCACAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCTCTA QVQLVQSGAEVKKPESVKVSKKASGYTFYNYGMNWRQAPGQGLEWMGWINTYTGEPYADDFKG RVTMSSDTSTSTAYLEINSLRSDDTAIYYCARWSWSDGYVYFDYWQGGTFTVTVSSGGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQKPKQPPKLLISWASTRE SGIPDRFSGSGSGTDFTLTIDSLQPEDSATYCYCQSAHFPITFTGQGRLEIKSGGGGSEVQLVESG GGILVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNIYATYYADSVKGRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNGFNSYVSWAYWQGTILTVSSGGGGSGGGSGGGGS QTVVTPQEPSLTVSPGGFTVLTLCGSSSTGAFTSGNYPNWVQKPKQAPRGLIGGTFKFLAPGTPARFSG SLLGKKAALTLISGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
16	CD33 AH3 HL x F12Q HL	artificial	nt	CAGGTGACGTGGTGACGCTGGAGCTGAGGTGAAAAAGCCTGGAGAGTCAGTCAAGGTCTCTCTGC AAGGCTAGCGGGTATACCTTCACAAAACCTATGGAATGAACTGGGTGAGGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACTACACTGGAGAGCCAAATATGCTGATGACTTCAAGGGA CGGTTACCATGTCTTCGGATACCTCTACACGACCTGCCTATTTGGAAAATCAACAGCCTCAGAAAT GATGACACGGCTATATATTTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGAC TACTGGGGCCAAAGGCACTACGGTCACCGTCTCCTCAGGTGGTGGTTCTTGGCGGCGCGGCTCC GGTGGTGGTGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCAAAGAAATAAGAACTCCCTTA GCTTGTACACAGAGAAAACAGGACAGCTCTCTAAATTAATCTCTTCTGGGCATCTACGCGGAA TCCGGGATCCCTGACCGATTCAGTGGCAGCGGCTCTGGACACAGATTCACCTCTCACTATTGACACG CTGACGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCCACTTCCCGATCACTTTGGC CAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGCTCCGAGGTGACGCTGGTCTGAGTCTGGA GGAGGATTGGTGACGCTGGAGGGTCAATTGAAAATCTCATGTGCAGCCTCTGGATTCACTTCAAT AGCTACGCCATGAACTGGGTCGCCAGGCTCCAGGAAAAGGTTTGGAAATGGGTGCTCGCATAGA AGTAAATATAATTAATGCAACATATATTGCCGATTTCAGTGAAAGGAGGTTACCATCTCCAGA GATGATTCAAAAACACTGCTCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAATAGTACGTTTCTTGGCGGCGCGGCTCCGGTGGTGGTTCT ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGTCTTGGCGGCGCGGCTCCGGTGGTGGTGGTTCT CAGACTGTTGTGACTCAGGAACTTCACTACCGTATCACTGGTGGAACAGTCACACTCACTTGT GGCTCCTCGACTGGGCTGTACATCTGGCAACTACCCAACTGGGTCCAAACAAAAACAGGTCTCAG GCACCCCGTGGTCTTAATAGGTGGACTAAGTTCCCTCGCCCCCGGTACTCTTCCAGAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGTACAGCCAGGATGAGGCAGAAATAT TACTGTGTCTCTATGGTACAGCAACCGCTGGGTGTCTCGGTGGAGGAACCAAACTGACTGTCTCTA
17	CD33 AH3 HL x I2C HL	artificial	aa	QVQLVQSGAEVKKPESVKVSKKASGYTFYNYGMNWRQAPGQGLEWMGWINTYTGEPYADDFKG RVTMSSDTSTSTAYLEINSLRSDDTAIYYCARWSWSDGYVYFDYWQGGTFTVTVSSGGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQKPKQPPKLLISWASTRE SGIPDRFSGSGSGTDFTLTIDSLQPEDSATYCYCQSAHFPITFTGQGRLEIKSGGGGSEVQLVESG GGILVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNIYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNGFNSYISWAYWQGTILTVSSGGGGSGGGSGGGGS

18	CD33 AH3 HL x I2C HL	artificial	nt	QTVVTFEPSTLVSPGGTVTLTTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAAAAGCCTGGAGAGTCAGTCAAGGTCTCTCTGC AAGGCTAGCGGGTATACCTTCACAACTATGGAATGAACTGGGTGAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGTCTTCGGATACCTCTACCAGCACTGCCTATTTGGAAATCAACAGCCTCAGAAAGT GATGACACGGCTATATATGTCGCGCTGGAGTTGGAGTGAGTGAGTTACTACGTTTACTTTGAC TACTGGGGCAAAGGCATACGGTCAACGCTCTCTCAGGTGGTGGTCTTGGCGCGCGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAG AGGACCACTCAACTGCAAGTCCAGCAGAGTGTCTTAGACAGCTCCAAAGATAAGAACTCCTTTA GCTTGGTACACAGAGAAAACAGGACAGCTCTCTAAATTTACTCTCTTCTGGGCATCTACGCGGAA TCCGGGATCCCTGACCGATTCTAGTGGCAGCGGTCTGGGACAGATTTCACTCTCACTATTGACAGC CTGCAGCTGAAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCACCTCCCGATCACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGTGGTCGAGTCTGGA GGAGGATTGGTGCAGCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTTGGAATCACCTTCAAT AAGTACGCCATGAACTGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAAATGGGTGCTCGCATAGA AGTAAATATAAATATGCAACATATTATGCCGATTCCAGTGAAGACAGGTTACCATCTCCAGA GATGATTCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAATAGTACATATCTTACTGGGCTTACTGGGGCCAAGGG ACTGTGGTCAACCGTCTCCTCAGGTGGTGGTGTCTTGGCGCGCGCGCTCCGGTGGTGGTGTCT CAGACTGTTGTGACTCAGGAACTTCACTACCGTATACCTGGTGGAAACAGTCACTCACTTGT GGCTCTCGACTGGGGCTGTACATCTGGCAACTACCCAAACTGGGTCCAAACAAACAGGTCAG GCACCCGCTGGTCTAAATAGGTGGACTAAGTCTTCCGCCCCGGTACTCTTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGTCTCTATGGTACAGCAACCGCTGGGTGTCTCGGTGGAGGAACCAACTGACTGTCTCTA QVQLVQSGAEVKKPGASVKVSKASGYTFITNYGMNWVKQAPGQGLKWMGWINTYITGEPTYADDFKG RVITMTSDTSTSTAYLELHNLRSDDDTAVYYCARWSWSVDGYVYFDYWGQGQTTVTVSS NYGMN
19	CD33 VH of AF5	artificial	aa	
20	CD33 HCDR1 of AF5	artificial	aa	
21	CD33 HCDR2 of AF5	artificial	aa	WINTYTGEPYADDFKG
22	CD33 HCDR3 of AF5	artificial	aa	WSWSVDGYVYFDY
23	CD33 VH of AF5	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGCGTCAGTCAAGGTCTCTCTGC AAGGCTAGCGGGTATACCTTCACAACTATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTTCGGATACCTCTTACCAGCACTGCCTATTTGGAACTCCACAACTCAGAAAGT

				GATGACACGGCTGTATATTACTGTGTGGCGGTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGGCACACGGGTACCGTCTCCTCA
24	CD33 VL of AF5	artificial	aa	DIVMTQSPDLSLTIVSLGERTTINCKSSQSVLDSKKNKNSLAWYQQKPGQPPKLLLSWASTRESGIPD RFSGSGSGTDFTLTIDSLQPEDSATYICQQSAHFPITFGQGTGLEIK
25	CD33 LCDR1 of AF5	artificial	aa	KSSQSVLDSKKNKNSLA
26	CD33 LCDR2 of AF5	artificial	aa	WASTRES
27	CD33 LCDR3 of AF5	artificial	aa	QQSAHFPIT
28	CD33VL of AF5	artificial	nt	GACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGACCAACCATCAAC TGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCAAGAAATAAGAACTCCTTAGCTTGGTACACAGCAG AAACAGGACAGCTCCTAAATTAATCTCCTTCTGGGCATCTACGCGGAAATCCGGGATCCCTGAC CGATTAGTGGCAGCGGTCTGGGACAGATTTCATCTCTACTATTGACAGCCTGCAGCCTGAAGAT TCTGCAACTTACTATTGTCAACAGTCTGCCCACCTTCCCGATCACCTTTGGCCAAAGGACACGACTG GAGATTAAA
29	CD33HL of AF5	artificial	aa	QVQLVQSGAEVKKPGASVKVSCKASGYTFITNYGMNFWKQAPGQGLKWMGWINTYTGEPYADDFKG RVMTSDTSTSTAYLELHNLRSDDTAVYICARWSWSDGYVYFDYWGQGTITVTVSSGGGSGGGGS GGGSDIVMTQSPDLSLTIVSLGERTTINCKSSQSVLDSKKNKNSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGSGTDFTLTIDSLQPEDSATYICQQSAHFPITFGQGTGLEIK
30	CD33 HL of AF5	artificial	nt	CAGGTGACAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGCGTCAGTCAAGGTCTCCTGC AAGGTAGCGGTATACCTTCACAACTATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGCT TTAAAAGTGGATGGGTGATAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTTCGGATACCTCTACACAGACTGCCTATTGGAACTCCACAACTCAGAAAT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGAC TACTGGGGCCAAAGGCACACTACGGTACCGTCTCCTCAGGTGGTGGTGTCTTGGCGGCGGCGGTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAG AGGACCACTCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAAGAAATAAGAACTCCTTA GCTTGGTACCAGAGAAACCAGGACAGCTCCTAAATTAATCTCTTCTGGGATCTACGCGGGA TCCGGGATCCCAGACCGATTGAGTGGCAGCGGCTTGGGACAGATTTCATCTCTACTATTGACAGC CTGACGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCACCTTCCCGATCACCTTTGGC CAAGGACACGACTGGAGATTAAA
31	CD33 AF5 HL x H2C HL	artificial	aa	QVQLVQSGAEVKKPGASVKVSCKASGYTFITNYGMNFWKQAPGQGLKWMGWINTYTGEPYADDFKG RVMTSDTSTSTAYLELHNLRSDDTAVYICARWSWSDGYVYFDYWGQGTITVTVSSGGGSGGGGS GGGSDIVMTQSPDLSLTIVSLGERTTINCKSSQSVLDSKKNKNSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGSGTDFTLTIDSLQPEDSATYICQQSAHFPITFGQGTGLEIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAAASGFTFNKYAMNFWKQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNLIKTEDTAVYICVRHGNFNSYISYWAYWGQGTITVTVSSGGGSGGGGSGGGGS QTVVTQEPSTVSPGGTITLTGCSSTGAVTSGYYPNFWVQQKPGQAPRGLIGGTFKFLAPGTPARFSG

32	CD33 AF5 HL x H2C HL	artificial	nt	SLLGKKAALTL SGVQPEDEAEFYCALWYSNRWVFGGTTKLTVIL CAGGTGCAGCTGGTGCAGTCTGGAGCTTGAGGTGAAGAAGCCTGGAGCGTCAAGTCAAGGTTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAAACATATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGTGGATAAAACACCTACACTGGAGAGCCAACATATGTGTGATGACTTCAAGGGA CGGGTTACCATGACTTCGGATACCTCTACACGACTGCCCTATTTGGAACCTCCACAACTCAGAAAGT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAGGCACCTACGGTCACCGTCTCCTCAGGTGGTGGTGTCTTGGCGGGCGGCTCC GGTGGTGGTGGTTCTTGACATCGTGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGGGCAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAAGAAATAAGAACTCCTTTA GCTTGGTACCAGAGAAAACAGGACAGCTCCTAAATTAATCTCTTCTTGGGCATCTACCGGGGAA TCCGGGATCCCTGACCGATTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGATCACCTTTGGC CTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGATCACCTTTGGC CAAGGGACACGACTGGAGATTAAATCCGAGGTGGTGGTCCGAGGTGCAGTGGTGCAGTCTGGA GGAGGATTGGTGCAGCCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAAT AAGTACGCCATGAAC TGGTCCGCCAGGCTCCAGGAAAGGTTTGGAAATGGTTGCTCGCATAAAGA AGTAAATATAATAATTAATGCAACATATTATGCCGATTCAAGTGAAGAACAGAGTTCAACCATCTCCAGA GATGATTCAAAAAACACTGCC TATCTACAAATGAACAACCTTGAAAACTGAGGACACTGCGCGTGAC TACTGTGTGAGACATGGGAACTTCGGTAAATAGTACATATCTTACTGGGCTTACTGGGGCCAAAGGG ACTCTGGTCAACCGTCTCCTCAGGTGGTGGTGGTCTTGGCGGGCGGCTCCGGTGGTGGTGGTCT CAGACTGTTGTGACTCAGGAACCTTCACTCAACCGTATCACTTGGTGAACAGTCACTCACTTGT GGCTCCTCGACTGGGGCTGTTACATCTGGCTACTACCCAACTGGGTCCAAACAAAACAGGTCAG GCACCCCGTGGTCTAATAGGTGGGACTAAGTCTCTGCCCCCGGTACTCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGTGCCCCTACCCCTCAAGGTTACAGGAGTACAGGAGTACAGGAGAAAT TACTGTGCTCTATGTTACAGCAACCGTGGGTGTTCTGGTGGAGAAACCAAACTGACTGTCTTA
33	CD33 AF5 HL x F12Q HL	artificial	aa	QVQLVQSGAEVKKPGASVKVSCKASGYTFITNYGMNWVKQAPGQGLKWMGWINTYTGEPYADDFKG RVMTSDTSTSTAYLELHNILRSDDTAVYICARWSWSDGYVYFDYWQQGTITVTVSSGGSGSGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSKNKNSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGSDTFTLTIDSLQPEDSATYYCQSAHFPITFGQGTRELEIKSGGGGSEVQLVLESG GGLVQPGGSLKLSCAAASGFTFNSYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKGRFTISR DDSKNTAYLQMNILKTEDTAVYCYVRHGNFNSYVSWWAYWQQGTILVTSSGGSGSGSGSGSGGGS QTVVTTQEP SLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGKKAALTL SGVQPEDEAEFYCVLWYSNRWVFGGTTKLTVIL
34	CD33 AF5 HL x F12Q HL	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTTGAGGTGAAGAAGCCTGGAGCGTCAAGTCAAGGTTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAAACATATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGTGGATAAAACACCTACACTGGAGAGCCAACATATGTGTGATGACTTCAAGGGA CGGGTTACCATGACTTCGGATACCTCTACACGACTGCCCTATTTGGAACCTCCACAACTCAGAAAGT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAGGCACCTACGGTCACCGTCTCCTCAGGTGGTGGTGTCTTGGCGGGCGGCTCC GGTGGTGGTGGTTCTTGACATCGTGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGGGCAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAAGAAATAAGAACTCCTTTA GCTTGGTACCAGAGAAAACAGGACAGCTCCTAAATTAATCTCTTCTTGGGCATCTACCGGGGAA TCCGGGATCCCTGACCGATTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGATCACCTTTGGC CTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGATCACCTTTGGC CAAGGGACACGACTGGAGATTAAATCCGAGGTGGTGGTCCGAGGTGCAGTGGTGCAGTCTGGA GGAGGATTGGTGCAGCCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAAT AAGTACGCCATGAAC TGGTCCGCCAGGCTCCAGGAAAGGTTTGGAAATGGTTGCTCGCATAAAGA AGTAAATATAATAATTAATGCAACATATTATGCCGATTCAAGTGAAGAACAGAGTTCAACCATCTCCAGA GATGATTCAAAAAACACTGCC TATCTACAAATGAACAACCTTGAAAACTGAGGACACTGCGCGTGAC TACTGTGTGAGACATGGGAACTTCGGTAAATAGTACATATCTTACTGGGCTTACTGGGGCCAAAGGG ACTCTGGTCAACCGTCTCCTCAGGTGGTGGTGGTCTTGGCGGGCGGCTCCGGTGGTGGTGGTCT CAGACTGTTGTGACTCAGGAACCTTCACTCAACCGTATCACTTGGTGAACAGTCACTCACTTGT GGCTCCTCGACTGGGGCTGTTACATCTGGCTACTACCCAACTGGGTCCAAACAAAACAGGTCAG GCACCCCGTGGTCTAATAGGTGGGACTAAGTCTCTGCCCCCGGTACTCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGTGCCCCTACCCCTCAAGGTTACAGGAGTACAGGAGTACAGGAGAAAT TACTGTGCTCTATGTTACAGCAACCGTGGGTGTTCTGGTGGAGAAACCAAACTGACTGTCTTA

35	CD33 AF5 HL x 12C HL	artificial	aa	AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTCTTTAGACAGCTCCAAAGAAATAAGAAATCCTTTA GCTTGGTACCAGCAGAAAAACAGGACAGCTCTCTAAATTAATCTCTCTTTCTGGGCATCTACGCGGAA TCCGGGATCCCTGACCGATTCAAGTGGCAGCGGTCTGGGACAGATTCTACTCTCTACTATTGACAGC CTGCAGCCTGAAGATTCTGCAACTTAATTAATGTAACAGTCTGCCACTTTCCCGATCACTTTGGC CAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGAGTGGTCTGAGTCTGGA GGAGGATTGGTGACGCTGGAGGTCAATGAAACTCTCATGTGAGCCTCTTGATTCACTTTCAAT AGCTACGCCATGAACTGGGTCCGCGCAGGTCCAGGAAAGGTTTGAATGGTGTCTCGCATAGA AGTAAATATAATAATATGCAACATATATGCCGATTCAATGAAAGGCAGGTTCACCATCTCCAGA GATGATCAAAAAACACTGCCTATCTACAAATGAACAATTTGAAACACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAATAGTACTGTTCTTGGTGGCTTACTTGGGGCCAAAGG ACTTGGTCACCGTCTCTCAGGTGGTGGTCTTGGCGGGCGGGTCCGGTGGTGGTGGTCTT CAGACTGTTGTGACTCAGGAACTTCACTCACCGTATCACTGGTGGAAACAGTCACTCACTTGT GGCTCCTCGACTGGGGCTGTTACATCTGGCAACTACCCAACTGGGTCCAAACAAACACAGGTGAG GCACCCCGTGGTCTAAATAGGTGGGACTAAGTCTCTGCCCCCGGTACTCTCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGATAAT TACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTTCGGTGGAGGAAACCAACTGACTGTCTCTA QVQLVQSGAEVKKPGASVKVSKASGYTFTNYGMNWKVQPGQLKWMGWINTYTGEPTIYADDFK RVMTSDTSTSTAYLELHNLRSDDTAVYYCARWSWSDGYVYFDYWGQGTITVTVSSGGGSGGGGS GGGSDIVMTQSPDLSLTSLGERITINCKSSQSLDSSKNKNSLAWYQKPGQPPKLLLSWASTRE SGIPDRFSGSGSDFTLTIDSLQPEDSATYCYQOQSAHFPITFGQGTRLFIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAA SGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNLLKTEDTAVYYCVRHGNFNSYISYWAYWGQGTILVTVSSGGGSGGGGSGGGGS QTVVTEPESLTVSPGGTITLTCSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGGKAALTLISGVQPEDEAEYYCVLMYSNRWVFGGGTKLTVL CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCTGGAGCGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAACTATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGT TTAAAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTTCGGATACCTTACCAGCACTGCCATTTTGGAACTCCACAACTCAGAACT GATGACACGGCTGTATATTACTGTGCGCTGGAGTTGGAGTGGTGTACTACGTTTACTTTGAC TACTGGGCGCAAGGCATACGCTACCGTCTCCTCAGGTGGTGGTGTCTGGCGCGCGGCTCC GGTGGTGGTGGTCTTGACATCGTGATGACACAGTGTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACTCAACTGCAAGTCCAGCAGAGTGTCTTAGACAGCTCCAAAGAAATAAGAAATCCTTTA GCTTGGTACAGCAGAAAAACAGGACAGCTCTCTAAATTAATTAATCTCTTCTGGGCATCTACGCGGAA TCCGGGATCCCTGACCGATTCACTGGCAGCGGTCTGGGACAGATTCTACTCTCACTATTGACAGC CTGCAGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCCATCTCCCGATCACTTTGGC CAAGGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGCTGGTGGTGGTGGGA GGAGGATTGGTGACGCTGGAGGCTCATTTGAAACTCTCATGTGAGCCTCTTGGAATTCACCTTCAAT AAGTACGCCATGAATGGGTCCCGCAGGCTCCAGGAAAGGTTTGGAAATGGGTGCTCTCGCATAGA AGTAAATATAATAATATGCAACATATATTATGCCGATTCAATGAAAGACAGGTTCACCATCTCCAGA
36	CD33 AF5 HL x 12C HL	artificial	nt	

					GATGATTCAAAAAACACTGCCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAATAGCTACATATCCTACTGGGCTTACTGGGGCCAAGGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTTCTTGGCGGCGCGGCTCCGGTGGTGGTTCT CAGACTGTTGTGACTCAGGAACCTTCACCTACCGTATCACCCTGGTGAACAGTCACACTCACTTGT GGCTCCTCGACTGGGGCTGTACATCTGGCAACTACCCAAACTGGGTCCAAACAAAAACCAGGTCAG GCACCCCGTGGTCTAATAGGTGGACTAAGTTCTCTGCCCGGCTACTCTGCCAGATTCTCAGGC TCCCTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGTTCTATAGGTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCTCTA QVQLVQSGAEVKKPGEISVKVSKASGYTFNRYGMNHWKQAPGQGLKWMGWINTYTGEPYADDFKG RVMTTDTSTSTAYMEIRNLNRNDDTAVYYCARWSWSDDGYVYFDYWGQGTTVTVSS
37	CD33 VH of AC8	artificial	aa		NYGMN
38	CD33 HCDR1 of AC8	artificial	aa		WINTYTGEPYADDFKG
39	CD33 HCDR2 of AC8	artificial	aa		WSWSDGYVYFDY
40	CD33 HCDR3 of AC8	artificial	aa		CAGGTGAGCTGGTGGAGCTGGAGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGCTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGCTGGATAAACACCTACACTGGAGAGCCAAATATGTGTGATGACTTCAAGGGA CGGTTACCATGACTACGGATACCTCTACCAGCACTGCCTATATGGAATCCGCAACCTCAGAAAT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGTGAGTTACTACGTTTACTTTGAC TACTGGGGCCAAAGGCACCTACGGTCACCGTCTCCTCA
41	CD33 VH of AC8	artificial	nt		DIVMTQSPDLSLTIVSLGERTTINCKSSQSVLDSKKNKNSLAWYQQKPGQPPKILLISWASTRESGIPD RFGSGSGTDFTLTIDSLQPEDSATYCYCQQSAHFPIITFGQGTREIK
42	CD33 VL of AC8	artificial	aa		KSSQSVLDSKKNKNSLA
43	CD33 LCDR1 of AC8	artificial	aa		WASTRES
44	CD33 LCDR2 of AC8	artificial	aa		QQSAHFPIIT
45	CD33 LCDR3 of AC8	artificial	aa		GACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAGAGGACCACCATCAAC TGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCAAGAAATAAGAACTCCTTAGCTTGGTACCAGCAG AAACCCAGGACAGCCTCCATAAATTACTCCTTTCTGGGCATCTACGCGGGAATCCGGGATCCCTGAC CGATTCAAGTGGCAGCGGCTCTGGACAGATTTCACTCTCACTATTGACAGCCTGCAGCCTGAAGAT TCTGCAACTTACTATTGTCAACAGTCTGCCCACTTCCCGATCACCTTTGGCCAAAGGACACGACTG
46	CD33 VL of AC8	artificial	nt		

47	CD33 HL of AC8	artificial	aa	GAGATTAAA QVQLVQSGAEVKKPESVKVSCKASGYTFNYGMNVWKQAPQQLKMWGWINITYTGEPTYADDFKG RVMTTDTSTSTAYMEIRNLRNDDTAVYICARWSWSDGYVYFDYWGQGTIVTVSSGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQOKPGQPPKILLISWASTRE SGIPDRFSGSGSDTFTLTIDSLQPEDSATYCYQOQSAHFPITFGQGTRELEIK CAGGTGACAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAACTATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGCTGGATAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTACGATACCTCTACAGCACTGCTATATGAAATCCGAACTCAGAAAT GATGACACGGCTGATATTAATGCTGCGCTGGAGTTGGAGTGATGGTTACTACTGTTACTTTGAC TACTGGGCAAGGCATACGGTACCGTCTCTCAGGTGGTGGTGGTCTTGGCGGCGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCATCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCAAAGAAAGAACTCCTTA GCTTGGTACCAGAGAAAACAGGACAGCTCTCTAAATTAATCTCTTCTGGCATCTACGCGGGA TCCGGGATCCCTGACCGATTGAGTGGCAGCGGCTCTGGGACAGATTCTACTCTACTATTGACAGC CTGACGCTGAAGATTCTGCACTTACTATTGTCACACAGTCTGCCCACCTTCCCGATCACCTTTGGC CAAGGACACGACTGGAGATTAAA
48	CD33 HL of AC8	artificial	nt	QVQLVQSGAEVKKPESVKVSCKASGYTFNYGMNVWKQAPQQLKMWGWINITYTGEPTYADDFKG RVMTTDTSTSTAYMEIRNLRNDDTAVYICARWSWSDGYVYFDYWGQGTIVTVSSGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQOKPGQPPKILLISWASTRE SGIPDRFSGSGSDTFTLTIDSLQPEDSATYCYQOQSAHFPITFGQGTRELEIK CAGGTGACAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAACTATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGCTGGATAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTACGATACCTCTACAGCACTGCTATATGAAATCCGCACTCAGAAAT GATGACACGGCTGATATTAATGCTGCGCTGGAGTTGGAGTGATGGTTACTACTGTTACTTTGAC TACTGGGCAAGGCATACGGTACCGTCTCTCAGGTGGTGGTGGTCTTGGCGGCGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCATCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCAAAGAAAGAACTCCTTA GCTTGGTACCAGAGAAAACAGGACAGCTCTCTAAATTAATCTCTTCTGGCATCTACGCGGGA TCCGGGATCCCTGACCGATTGAGTGGCAGCGGCTCTGGGACAGATTCTACTCTACTATTGACAGC CTGACGCTGAAGATTCTGCACTTACTATTGTCACACAGTCTGCCCACCTTCCCGATCACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGTCCGAGGCTCTGGATTCAGCTTCAAT GGAGGATTGGTGCAGCTGGAGGGTCAATTGAAACTCTCATGTGACGCTCTGGATTCACCTTCAAT AAGTACGCCATGAACCTGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAAATGGGTGCTCGCATAGA
49	CD33 AC8 HL x H2C HL	artificial	aa	QVQLVQSGAEVKKPESVKVSCKASGYTFNYGMNVWKQAPQQLKMWGWINITYTGEPTYADDFKG RVMTTDTSTSTAYMEIRNLRNDDTAVYICARWSWSDGYVYFDYWGQGTIVTVSSGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQOKPGQPPKILLISWASTRE SGIPDRFSGSGSDTFTLTIDSLQPEDSATYCYQOQSAHFPITFGQGTRELEIKSGGGSEVQLVESG GGLVQPGGSLKLSAASGFTFNKYAMNVWRQAPGKLEWVARIRSKYNNYATYADSVKDRFTISR DDSKNTAYLQMNLLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTIVTVSSGGGSGGGGSGGGGS QTVVTEPESLTVSPGGTIVLTCTGSSTGAVTSGYYPNVWQOKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGKKAALTLISGVQPEDEAEYYCALWYSNRWVFGGKTLTVL
50	CD33 AC8 HL x H2C HL	artificial	nt	CAGGTGACAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAACTATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGCTGGATAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTACGATACCTCTACAGCACTGCTATATGAAATCCGCACTCAGAAAT GATGACACGGCTGATATTAATGCTGCGCTGGAGTTGGAGTGATGGTTACTACTGTTACTTTGAC TACTGGGCAAGGCATACGGTACCGTCTCTCAGGTGGTGGTGGTCTTGGCGGCGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCATCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCAAAGAAAGAACTCCTTA GCTTGGTACCAGAGAAAACAGGACAGCTCTCTAAATTAATCTCTTCTGGCATCTACGCGGGA TCCGGGATCCCTGACCGATTGAGTGGCAGCGGCTCTGGGACAGATTCTACTCTACTATTGACAGC CTGACGCTGAAGATTCTGCACTTACTATTGTCACACAGTCTGCCCACCTTCCCGATCACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGTCCGAGGCTCTGGATTCAGCTTCAAT GGAGGATTGGTGCAGCTGGAGGGTCAATTGAAACTCTCATGTGACGCTCTGGATTCACCTTCAAT AAGTACGCCATGAACCTGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAAATGGGTGCTCGCATAGA

				AGTAAATATAATAATATGCAACATATATATGCCGATTAGTGAAGACAGAGTTTACCATCTCCAGA GATGATTCAAAAACACTGCCATATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGAGACATGGGAACCTTCGGTAATAGTACATATCTTACTTGGCTTACTTGGGGCCAAAGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTCTTGGCGCGCGGCTCCGGTGGTGGTGGTCTT CAGACTGTTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGAACAGTCACTCACTTGT GGCTCCTCGACTGGGGCTGTACATCTGGCTACTACCCAACTGGGTCCAACAAAAACAGGTGAG GCACCCCGTGGTCTAAATAGGTGGACTAAATCTCTGCCCGGTACTCTGCCAGATCTCAGGC TCCCCTGCTTGGAGGCAAGGCTGCCCTCACCCCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAATAT TACTGTGCTCTATGGGTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCTCTA
51	CD33 AC8 HL x F12Q HL	artificial	aa	QVQLVQSGAEVKKPESVKYSCKASGYTFNRYGMNWKQAPGQGLKWMGWINTYTGEPYADDFKG RVMTTDTSTSTAYMEIRNLRNDDTAVYYCARWSWSDGYVYFDYWGQGTFTVTVSSGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLSDSKNKNLSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGGTDFLTIDSLQPEDSATYYCQQSAHFPITFGQGTREIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAAASGFTFNSYAMNWRQAPGKGLEWVARIRSKYNNIYATYYADSVKGRFTISR DDSKNTAYLQMNNLKTEDTAVYYCVRHGNFNSYVSWWAYWGQGTFLVTVSSGGGSGGGGSGGGGS QTIVTQEP SLTVSPGGTIVTLITCGSSTGAVTSGNYPNWKQKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGGKAAALTL SGVQPEDEAEFYCVLMYSNRWVFGGKLTIVL
52	CD33 AC8 HL x F12Q HL	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGTATACCTTCACAAAATATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAAGTGGATGGGTGATATAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTACGGATACCTCTACCAGCACTGCCCTATATGGAATCCGCAACCTCAGAAAT GATGACACGGCTGTATATTAATGTGCGCGCTGGAGTTGGAGTGTGAGTTACTAGTTTACTTTGAC TACTGGGCGCAAGCACTACGGTACCGTCTCCTCAGGTGGTGGTCTTGGCGGCGGGCTCC GGTGGTGGTGGTCTTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCAACATCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCAAGAAATAAGAACTCCTTA GCTTGGTACCAGAGAAACAGGACAGCTCTTAAATTAATCTCTTCTTGGCATCTACGCGGAA TCCGGGATCCCTGACCGATTCACTGGCAGCGGGTCTGGGACAGATTCACTCTCACTATTGACAGC CTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGATCACCTTTGGC CAAGGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGCTGGTCGAGTCTGGA GGAGGATTGGTGAGCTGGAGGTTCATTGAAAATCTCATGTGCAGCTCTGGATTCACTTCAAT AGCTACGCCATGAACCTGGGTCCGCGCAGGCTCCAGGAAAGGGTTTGGAAATGGGTTCGCTCGATAAGA AGTAAATATAATAATAATATGCAACATATATATGCCGATTAGTGAAGAGCAGGTTTACCATCTCCAGA GATGATTCAAAAACACTGCCATATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACCTTCGGTAATAGTACGTTTCTTGGTGGCTTACTTGGGGCCAAAGG ACTCTGGTCAACCGTCTCCTCAGGTGGTGGTGGTCTTGGCGGCGGGCTCCGGTGGTGGTCTT CAGACTGTTGTGACTCAGGAACCTTCACTACCGTATCACTTGGTGAACAGTCACTCACTTGT GGCTCCTCGACTGGGGCTGTATACATCTGGCAACTACCCAACTGGGTCCAACAAAAACAGGTGAG GCACCCCGTGGTCTAAATAGGTGGACTAAGTTCTCTGCCCGGTACTCTTCCAGATTCTCAGGC TCCCCTGCTTGGAGGCAAGGCTGCCCTCACCCCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAATAT

53	CD33 AC8 HL x I2C HL	artificial	aa	TACTGTGTTCTATGGTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCTCTA QVQLVQSGAEVKKPESVKVSCKASGYFTNYGMNWKQAPGQGLKWMGWINTYTGEPYADDFKG RVMTTDTSTSTAYMEIRNLNDDTAVYYCARWSWDGYVYFDYWGQGTITVTVSSGGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQOKPGQPPKLLLSWASTRE SGIPDRFSGSGSDTFTLTIDSLQPEDSATYCYQSAHFPITTFGQGTRLFEEKSGGGSEVQLVESG GGILVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNIYATYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTITVTVSSGGGGSGGGSGGGGS QTIVTQEPSLTVSPGGTFTLTTCGSTGAVTSGNYPNWKQAPGQAPRGLIGGTGKFLAPGTPARFSG SLLGKKAALTLISGVQPEDEAEYYCVLMYSNRWVFGGGTKLTVL
54	CD33 AC8 HL x I2C HL	artificial	nt	CAGGTGCAGCTGGTGTCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGTGGATAAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTACGGATACCTCTACCAGCACTGCCATATATGGAATCCGCAACCTCAGAAAT GATGACACGGCTGTATATTAATGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGAC TACTGGGGCCAAAGGCATACGGTCACCGTCTCCTCAGGTGGTGGTTCTTGGCGGGCGGCTCC GGTGGTGGTGGTTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCAAGAATAAGAACTCCCTTA GCTTGGTACCAGAGAAAACAGGACAGCTCCTAAATTAATCTCTTCTGGGCATCTACGCGGGAA TCCGGGATCCCTGACCGGATTCAGTGGCAGCGGTCTGGGACAGATTTCACTCTCACTATTGACAGC CTGCAGCCTGAAAGATTCTGCAACTTACTATTTGTCAACAGTCTGCCCACTTCCCGATCACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGCTCCGAGGTGACGTGGTTCGAGTCTGGA GGAGGATTGGTGACGCTGGAGGGTCAATTGAAACTCTCATGTGCAGCTCTTGGAATTCACCTTCAAT AAGTACCCCATGAACTGGGTCCCGCAGGCTCCAGGAAAGGGTTTGGAATGGGTGCTCGCATAGA AGTAAATATAATAATATGCAACATATTAATGCCGATTTCAGTGAAAGACAGGTTACCATCTCCAGA GATGATTCAAAAAACACTGCCATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACCTTCGGTAATAGCTACATATCCTTACTGGGCTTACTGGGGCCAAAGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGTCTTGGCGCGCGCGCTCCGGTGGTGGTGGTCTT CAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGAACAGTCACACTCACTTGT GGCTCCTCGACTGGGGCTGTACATCTGGCAACTACCCAACTGGGTCCAAACAAAAACCAAGTCAG GCACCCCGCTGGTCTAATAGGTGGACTAAAGTTCCCTCGCCCCGGTACTCCTGTCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGTGCCCTCACCCCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCTCTA TACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCTCTA
55	CD33 VH of AH11	artificial	aa	QVQLVQSGAEVKKPESVKVSCKASGYFTNYGMNWKQAPGQGLKWMGWINTYTGEPYADDFKG RVMTSDTSTSTAYMEISSLRSDDTAVYYCARWSWDGYVYFDYWGQGTITVTVSS
56	CD33 HCDR1 of AH11	artificial	aa	NYGMN
57	CD33 HCDR2 of AH11	artificial	aa	WINTYTGEPYADDFKG

58	HCDR3	artificial	aa	WSWSDGYVYVFDY
59	CD33 VH of AH11	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAAACATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAAGTGGATGGCTGGATAAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTTCGGATACCTCTACACAGCACTGCCCTATATGGAATCAGCAGCCTCAGAAAT GATGACACGGCTGTATATTAATCTGTGCGCTGGAGTTGGAGTATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGCACTACGGTCACCGTCTCCTCA
60	CD33 VL of AH11	artificial	aa	DIVMTQSPDSLTVSLGERTTINCKSSQSVDSSKNKNSLAWYQQKPGQPPLKLLLSWASTRESGIPD RFSGSGGTDFLTIDSLQPEDSATYYCQSAHFPIITFGQGTRLEIK
61	CD33 LCDR1 of AH11	artificial	aa	KSSQSVLDSSKNKNSLA
62	CD33 LCDR2 of AH11	artificial	aa	WASTRES
63	CD33LCDR3 of AH11	artificial	aa	QQSAHFPIIT
64	CD33 VL of AH11	artificial	nt	GACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGACCACCATCAAC TGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCAAGAAATAAGAACTCCTTAGCTTGGTACCAGCAG AAACCAGGACAGCCTCCTAAATTAATCTCTTCTTGGGCATCTACGCGGGAATCCGGGATCCCTGAC CGATTGAGTGGCAGCGGGTCTGGGACAGATTTCACTCTCACTATTGACAGCCTGCAGCCTGAAGAT TCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGATCACCTTTGGCCAAAGGACACAGACTG GAGATTAAA
65	CD33 HL of AH11	artificial	aa	QVQLVQSGAEVKKPGEISVKVSKASGYTFITNYGMNWVKQAPGQGLKMMGWINTYTGEPYADDFKG RVTMTSDTSTSTAYMEISSLRSDDTAVYICARWSWSDGYVYFDYWGQGTITVTVSSGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVDSSKNKNSLAWYQQKPGQPPLKLLLSWASTRE SGIPDRFSGSGGTDFLTIDSLQPEDSATYYCQSAHFPIITFGQGTRLEIK
66	CD33 HL of AH11	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGCTAGCGGGTATACCTTCACAAAACATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAAGTGGATGGCTGGATAAAACACCTACACTGGAGAGCAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTTCGGATACCTCTACACAGCACTGCCCTATATGGAATCAGCAGCCTCAGAAAT GATGACACGGCTGTATATTAATCTGTGCGCTGGAGTTGGAGTATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGCACTACGGTCACCGTCTCCTCAAGTGGTGGTGTCTTGGCGGCGGCTCC GGTGGTGGTGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCAAGAAATAAGAACTCCCTTA GCTTGTGTTACCAAGCAAAACAGGACAGCTCCCTAAATTAATCTCTTCTGGGCATCTACGCGGGA TCCGGGATCCCTTGACCGATTACGTGGCAGCGGTCTGGGACAGATTTCAC'TCTCACTATTGACAGC CTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCACTTCCCGATCACCTTTGGC

67	CD33 AH11 HL x H2C HL	artificial	aa	CAAGGACACGACTGGAGATTAAA QVQLVQSGAEVKKPESVKVSCKASGYTFITNYGMNVWKQAPGQGLKWMGWINTYITGEPTYADDFKG RVMTSDTSTSTAYMEISSLRSDDTAVYYCARWSWSDGYVYFDYWQGTITVTVSSGGSGSGSGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQOKPGQPPKLLLSWASTRE SGIPDRFSGSGSGTDFTLTIDSLQPEDSATYCYCQSAHFPIITFGQGTREIKSGGGGSEVQLVESG GGILVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNIYATYADSVKGRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNFGNSYISYWAYWGQGLTVTVSSGGSGSGSGSGSGGS QTVVTQEPSTLTVSPGGTVTLITCGSSTGAVTSGYYPNWVQOKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTLISGVQPEDEAEYYCALWYSNRWVFGGTPKLTIVL
68	CD33 AH11 HL x H2C HL	artificial	nt	CAGGTGCAGCTGGTGAGCTGAGGTGAAGAAAGCCTTGGAGAGTCAGTCAAGGTCCTCTCTGC AAGGCTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCCAAACATATGCTGATGACTTCAAGGGA CGGTTACCATGACTTCGGATACCTCTACCAGACACTGCCATATATGGAATACAGACCTCAGAAAT GATGACACGGCTGTATATTAATGTGCGCGCTGGAGTTGGAGTGTGCTTACTACGTTTACTTTTAC TACTGGGGCCAAAGGCATACGGTCACCGTCTCTCTCAGGTGGTGGTGGTCTTGGCGGCGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCAAGAATAAGAACTCCCTTA GCTTGGTACCAGAGAAAACAGGACAGCCTCCTAAATTAATCTCTTCTCTGGGCATCTACGCGGGAA TCCGGGATCCCTGACCGGATTCAGTGGCAGCGGCTCTGGACAGATTTCACTCTCACTATTGACAGC CTGCAGCCTGAAAGATTCTGCAACTTACTATTTGCAACAGTCTGCCCATCTCCCGATCACCTTTTGGC CAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGCTCCGAGGTGCAGCTGGTTCAGTCTGGA GGAGGATTGGTGACGCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAAT AAGTACGCCATGAACTGGGTCGCCAGGCTCCAGGAAAAGGTTTGGAAATGGGTGTCTCGCATAGA AGTAAATATAATAATATGCAACATATTAATGCCGATTAGTGAAGACAGGTTACCATCTCCAGA GATGATTCAAAAAACACTGCCATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACCTTCGGTAATAGCTACATATCTTACTTGGGCTTACTTGGGGCCAAAGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGTCTTGGCGGCGCGGCTCCGGTGGTGGTGGTCTT CAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGAACAGTCACACTCACTTGT GGCTCCTCGACTGGGGCTGTACATCTGGCTACTACCCAAACTGGGTCCAACAAAAACAGGTCAG GCACCCCGCTGGTCTAATAGGTGGACTAAAGTTCTTCCCGCCCGGTACTCTCTGCAGATTCTCAGGC TCCCTGTCTGGAGGCAAGGCTGCCCTCACTCCCTCTCAGGGGTGAGCCAGAGGATGAGGCAGAAATAT TACTGTGCTCTATGGTACAGAACCGCTGGGTGTTCGGTGGAGGAACCAAACTGACTGTCTCTA
69	CD33 AH11 HL x F12Q HL	artificial	aa	QVQLVQSGAEVKKPESVKVSCKASGYTFITNYGMNVWKQAPGQGLKWMGWINTYITGEPTYADDFKG RVMTSDTSTSTAYMEISSLRSDDTAVYYCARWSWSDGYVYFDYWQGTITVTVSSGGSGSGSGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQOKPGQPPKLLLSWASTRE SGIPDRFSGSGSGTDFTLTIDSLQPEDSATYCYCQSAHFPIITFGQGTREIKSGGGGSEVQLVESG GGILVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNIYATYADSVKGRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNFGNSYISYWAYWGQGLTVTVSSGGSGSGSGSGSGGS QTVVTQEPSTLTVSPGGTVTLITCGSSTGAVTSGYYPNWVQOKPGQAPRGLIGGTKFLAPGTPARFSG

70	CD33 AH11 HL x F12Q HL	artificial	nt	SLLGGKAAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCCAAACATATGCTGATGACTTCAAGGGA CGGGTTACCATGACTTCGGATACCTCTACCAGCACTGCCTATATGGAATTCAGCAGCCTCAGAAAGT GATGACACGGCTGTATATTAATGCTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGGCATACGGTACCGTCTCCTCAGGTGGTGGTCTTGGCGCGCGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAAACTGCAAGTCCAGCCAGAGTGTTTATGACAGCTCCAAAGAAATAAGAACTCCTTTA GCTTGGTACACAGAGAAAACAGGACAGCCTCCTAAAATTAATCTCTCTTCTGGGCATCTACGCGGGA TCCGGGATCCCTGACCGATTAGTGGCAGCGGGTCTGGGACAGATTTACTCTACTATTTGACAGC CTGACGCTGAAAGATTCTGCAACTTACTATTTGTCAAACAGCTTGCCCACTTCCCGATCACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGTGGTGCAGTCTGGA GGAGGATTGGTCAGCCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTTCAAT AGCTACGCCATGAACTGGGTCCGCCAGGCTCCAGGAAAAGGTTTGGAAATGGGTGCTCGCATAGA AGTAAATATAAATAATATGCAACATATATGCCGATTAGTGAAGGAGGTTTCCATCTCCAGAT GATGATTCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAATAGCTACGTTTCTGGCGCGCGGCTCCGGTGGTGGTCTT ACTCTGGTCAACCGTCTCCTCAGGTGGTGGTCTTGGCGCGCGGCTCCGGTGGTGGTCTT CAGACTGTTGTGACTCAGGAACTTCACTACCGTATCACTGGTGGAAACAGTCACACTCACTTGT GGCTCTCGACTGGGCTGTACATCTGGCAACTACCCAACTGGGTCCAAACAAAACAGGTTCAG GCACCCGCTGGTCTAATAGGTGGGACTAAGTCTCTGCCCCCGTACTCTCTGCCAGATTCTCAGGC TCCCCTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGTTCTATGGTACAGCAACCGCTGGGTGTTTCGGTGGAGGAAACCAAACTGACTGTCTCTA
71	CD33 AH11 HL x I2C HL	artificial	aa	QVQLVQSGAEVKKPESVKVSKASGYTFNYGMNWVKQAPGQGLKWMGWINTYTGEPYADDFKG RVMTSDTSTSTAYMEISSLRSDDTAVYICARWSWDGYVYFDYWGQGTITVTVSSGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGSDTFTLTIDSLQPEDSATYCYQQSAHFPITFGQGTREIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNIYATYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYICVRHGNFGNSYISWAYWGQGTITVTVSSGGGSGGGGSGGGGS QTVVTQEPSTLTVSPGGFVTLTCGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKLAPGTPARFSG SLLGGKAAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
72	CD33 AH11 HL x I2C HL	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAAAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCCAAACATATGCTGATGACTTCAAGGGA CGGGTTACCATGACTTCGGATACCTCTACCAGCACTGCCTATATGGAATTCAGCAGCCTCAGAAAGT GATGACACGGCTGTATATTAATGCTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGGCATACGGTACCGTCTCCTCAGGTGGTGGTCTTGGCGCGCGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG

				AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAAAGAAATAAGAACTCCTTTA GCTTGGTACCAGCAGAAAAACAGGACAGCCTCCTAAATTAATCTCTCTTTCTGGGCATCTACGCGGAA TCCGGGATCCCTGACCGATTCAAGTGGCAGCGGGTCTGGGACAGATTCTACTCTCACTATTGACAGC CTGCAGCCTGAAGATTCTGCAACTTAATTAATGTAACAGCTTGCCCACTTCCCGATCACTTTGGC CAAGGACACGACTGGAGATTAAATCCGAGGTGGTGCTCCGAGGTGAGCTGGTCGAGTCTGAAT GGAGGATTGGTGACGCTGGAGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAAT AAGTACGCCATGAACTGGGTCCGACAGCTCCAGGAAAGGGTTTGAATGGGTGCTCGCATAAAGA AGTAAATATAATAATATGCAACATATATGCGGATTCAGTGAAGACAGGTTTACCATCTCCAGA GATGATCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTTCGGTAATAGTACATATCTCTACTGGGCTTACTTGGGGCCAAAGG ACTCTGGTCACCGTCTCTCAGGTGGTGGTGTCTGGCGGGCGGGTCCGGTGGTGGTGTCT CAGACTGTTGTGACTCAGGAACTTCACTCACCGTATCACTGGTGGAAACAGTCACTCACTTGT GGCTCCTCGACTGGGGCTGTTACATCTGGCAACTACCCAACTGGGTCCAAACAAAAACAGGTCAG GCACCCCGTGGTCTAAATAGGTGGGACTAAGTCTCTCGCCCCGGTACTCTCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTTCGGTGGAGGAAACCAACTGACTGTCTCTA
73	CD33 VH of B3	artificial	aa	QVQLVQSGAEVKKPGESVKVSKCKASGYTFITNYGMNWKQAPGQGLEWMGWINTYTGETNYADKFFQG RVFTSTSTSTAYMELRNLIKSDDTAVYYCARWSWSDDGYVYFYFDYWGQGTITVTVSS
74	CD33 HCDR1 of B3	artificial	aa	NYGMN
75	CD33 HCDR2 of B3	artificial	aa	WINTYTGETNYADKFFQG
76	CD33 HCDR3 of B3	artificial	aa	WSWSDDGYVYFYDY
77	CD33 VH of B3	artificial	nt	CAGGTGCAGCTGGTGCAGCTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGACAAAATATGCTGATAAGTTCAGGGA CGCGTTACCTTCACTTCGGATACCTCTACCAGCACTGCCTATATGGAACCTCCGCAACCTCAAAAGT GATGACACGGCTGTATATTAATGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGGCACCTACGGTCACCGTCTCCTCA
78	CD33 VL of B3	artificial	aa	DIVMTQSPDMSMTVSLGERTTINCKSSQSVLDSSTNKNLSLAWYQQKPGQPPKILLISWASTRESGIPD RFSGSGSGTDFTLTIDSLQPEDSATYFCQQSAHFPIITFGQGTRLDIK
79	CD33 LCDR1 of B3	artificial	aa	KSSQSVLDSSTNKNLSLA
80	CD33 LCDR2 of B3	artificial	aa	WASTRE
81	CD33LCDR3 of B3	artificial	aa	QQSAHFPIIT
82	CD33 VL of B3	artificial	nt	GACATCGTGAATGACACAGTCTCCAGACTCCATGACTGTGTCTCTTGGGCGAGAGGACCACCATCAAC TGCAAGTCCAGCCAGAGTGTTTTTAGACAGCTCCACGAAATAAGAACTCCTTAGCTTGGTACCAGCAG

				AAAACAGGACAGCCTCCTAAATTTACTCCTTTCTTGGGCATCTACGCGGGAATCCGGGATCCCTGAC CGATTGAGTGGCAGCGGCTTGGGACAGATTTCACTCTCACTATTGACAGCCTGCAGCCTGAAGAT TCTGCAACTTACTATTGTCAACAGCTTGCCCACTTCCCGATCACCTTTGGCCAAAGGACACGACTG GACATTAAA
83	CD33 HL of B3	artificial	aa	QVQLVQSGAEVKKPGEISVKVSKASGYTFITNYGMNWVKQAPGQGLEWMGWINTYTGENTNYADKFKQG RVFTFTSDTSTAYMELRNILKSDDTAVYYCARWSWSDGYVYFDYWGQGTFTVTVSSGGGSGGGGS GGGSDIVMTQSPDSMTVSLGERTTINCKSSQSVLDSSTNKNLSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGSGTDFTLTIDSLQPEDSATYFCQQSAHFPITFGQGRLLDIK
84	CD33 HL of B3	artificial	nt	CAGGTGCAGCTGGTGACGCTTGAGAGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTTCCTGC AAGGCTAGCGGGTATACCTTCACAAAATATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGACAAAATATGCTGATAAGTTCCAGGGA CGGTTACCTTCACTTCGGATACCTTACCAGCAGCTGCTATATGGAACCTCCGCAACCTCAAAAGT GATGACACGGCTGTATATTTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGAC TACTGGGCGCAAGGCACCTACGGTCACCGTCTCCTCAGGTGGTGGTCTTGGCGGGCGGCTCC GGTGGTGGTGGTTCTGACATCGTGATGACACAGCTCCAGACTCCATGACTGTGTCTCTGGCGGAG AGGACCAACATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCACGAATAAGAACTCCTTA GCTTGGTACCAGAGAAAACAGGACAGCCTCCTAAATTTACTCCTTTCTTGGGCATCTACGCGGGA TCCGGGATCCCTGACCGATTGAGTGGCAGCGGCTGGGACAGATTTCACTCTCACTATTGACAGC CTGCAGCCTGAAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGATCACCTTTGGC CAAGGACACGACTGGACATTAAA
85	CD33 B3 HL x H2C HL	artificial	aa	QVQLVQSGAEVKKPGEISVKVSKASGYTFITNYGMNWVKQAPGQGLEWMGWINTYTGENTNYADKFKQG RVFTFTSDTSTAYMELRNILKSDDTAVYYCARWSWSDGYVYFDYWGQGTFTVTVSSGGGSGGGGS GGGSDIVMTQSPDSMTVSLGERTTINCKSSQSVLDSSTNKNLSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGSGTDFTLTIDSLQPEDSATYFCQQSAHFPITFGQGRLLDIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAAAGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGTFGNSYISYWAYWGQGTFTVTVSSGGGSGGGGSGGGGS QTVVTFEPSTLVSPGGTFTLTGSSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGGKAALLTLGSGVQPEDEAEFYCALWYSNRWVFGGTKLTVL
86	CD33 B3 HL x H2C HL	artificial	nt	CAGGTGCAGCTGGTGACGCTTGAGAGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTTCCTGC AAGGCTAGCGGGTATACCTTCACAAAATATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGACAAAATATGCTGATAAGTTCCAGGGA CGGTTACCTTCACTTCGGATACCTTACCAGCAGCTGCTATATGGAACCTCCGCAACCTCAAAAGT GATGACACGGCTGTATATTTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGAC TACTGGGCGCAAGGCACCTACGGTCACCGTCTCCTCAGGTGGTGGTGGTCTTGGCGGGCGGCTCC GGTGGTGGTGGTTCTGACATCGTGATGACACAGCTCCAGACTCCATGACTGTGTCTCTGGCGGAG AGGACCAACATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCACGAATAAGAACTCCTTA GCTTGGTACCAGAGAAAACAGGACAGCCTCCTAAATTTACTCCTTTCTTGGGCATCTACGCGGGA TCCGGGATCCCTGACCGATTGAGTGGCAGCGGCTGGGACAGATTTCACTCTCACTATTGACAGC CTGCAGCCTGAAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGATCACCTTTGGC

					CAAGGGACACGACTGGACATTAAATCCGGAGGTGGTGGCTCCGAGGTGCAGCTGGTCGAGTCTGGAGGATTGGTGCAGCCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAAT AAGTACGCCATGAACCTGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAAATGGGTTGCTCGCATAAAGA AGTAAATATAATAATTATGCAACATATTATGCCGATTAGTGAAGACAGAGTTTACCATCTCCAGA GATGATTCAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGAACTTCGGTAATAGTACATATCTACTGGGCTTACTGGGCGCAAGGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGTCTTGGCGCGCGGCTCCGGTGGTGGTGTCT CAGACTGTGTGACTCAGGAACCTTCACCTACCGTATCACCTGGTGGAAACAGTCACTCACTTGT GGCCTCTCGACTGGGGCTGTACATCTGGCTACCCAAACTGGGTCCAACAAAAACAGGTTCAG GCACCCCGTGTCTAAATAGGTGGGACTAAGTTCTTCGCCCCCGGTACTCTTGCCAGATTCTCAGGC TCCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGGATGAGGCAGAAATAT TACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTCCGTGGAGGAACCAAACTGACTGTCTCTA
87	CD33 B3 HL x F12Q HL	artificial	aa		QVQLVQSGAEVKKPGEISVKVSKKASYFTFTNYGMNVWKQAPQQLGLEWMGWINTYTGENTYADKFQGRVFTSDTSTSTAYMELRNILKSDDTAVYYCARWSWSDGYVYFDYWGQGTITVTVSSGGGSGGGSGSGGSDIVMTQSPDSMTVSLGERTTINCKSSQSVLDSSTNKNSLAWYQKPGQPPKLLLSWASTRESGIPDRFSGSGSDTFTLTIDSLQPEDSATYCYQQSAHFPITFGQGTRLDIKSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNSYAMNVRQAPGKGLEWVARIRSKYNNIYATYADSVKGRFTISRDDSKNTAYLQMNILKTEDTAVYYCVRHGNGFNSYVSWWAYWGQTLTVTVSSGGGSGGGGSGGGSGQTIVTQEPSTLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKLAPGTPARFSGSLLGGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTFKLTVL
88	CD33 B3 HL x F12Q HL	artificial	nt		CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAACCTTGAGAGTCAAGGTCTCCTTCGCAAGGCTAGCGGGTATACCTTCACAAAACATATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGGTTTAGAGTGGATGGGTGGATAAAACACCTACACTGGAGAGACAAAACATATGCTGATAAGTTTCAGGGA CGCGTTACCTTCACTTCGGATACCTCTACCAGCACTGCCATATATGAACTCCGCAACCTCAAAAAGT GATGACACGGCTGTATATTACTGTGCGGCTGGAGTTGGAGTGTACTACGTTTACTTTGAC TACTGGGGCCAAAGCACTACGGTCACCGTCTCCTCAGGTGGTGGTGTCTTGGCGGCGGGCTCC GGTGGTGGTGTCTTGACATCGTGATGACACAGTCTCCAGACTCCATGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGTCCACGAATAAGAACTCCTTA GCTTGGTACCAGAGAAAACAGGACAGCTCTCTAAATTACTCTTCTTCTGGGCATCTACGCGGGA TCCGGGATCCCTGACCGATTCAAGTGGCAGCGGCTGGGACAGATTTCACTCTCACTATTGACAGC CTGCAGCTTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCAGATCACCTTTGGC CAAGGGACACGACTGGACATTAAATCCGGAGGTGGTGGCTCCGAGGTGCAGCTGGTCGAGTCTGGA GGAGGATTGGTGCAGCCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAAT AGCTACGCCATGAACCTGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAAATGGGTTGCTCGCATAAAGA AGTAAATATAATAATTATGCAACATATTATGCCGATTAGTGAAGGCAAGGTTTCACTATCCAGA GATGATTCAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGAACTTCGGTAATAGTACGTTCTTCTGGCGCGGCTTACTGGGCGCAAGGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGTCTTGGCGCGCGGCTCCGGTGGTGGTGTCT CAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGGAAACAGTCACTCACTTGT

89	CD33 B3 HL x I2C HL	artificial	aa	GGCTCCTCGACTGGGGCTGTTACATCTGGCAACTACCCAAACTGGGTCCAACAAAAACCAGGTCAG GCACCCCGTGGTCTAAATAGGTGGGACTAAGTTCTTCGCCCCCGGTACTCCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCTCTTA QVQLVQSGAEVKKPGEISVKVSKKASGYTFNYGMNWKQAPGQGLEWMGWINTYTGFTNYADKFKQ RVFTFTSDTSTAYMELRNILKSDDTAVYYCARWSWSGDYVYFDYWGQGTFTVTVSSGGGSGGGGS GGGSDIVMTQSPDSMTVSLGERTTINCKSSQSVLSDSTNKNLSLAWYQKPKGPPKLLLSWASTRE SGIPDRFSGSGSDFTLTIDSLQPEDSATYCYQOQSAHFPITFGQGTDLIDIKSGGGSEVQLVESG GGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLLVTVSSGGGSGGGSGGGGS QTVVTEPSLTVSPGGTVTLTTCGSSTGAVTSNYPNWVQKPKGAPRGLIGGTFKLAPGTPARFSG SLLGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGKTLTVL
90	CD33 B3 HL x I2C HL	artificial	nt	CAGGTGACGCTGGTGACGCTGGAGCTGAGGTGAAGAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTTCACAAAATATGGAAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGTGGATAAACACCTACACTGGAGAGACAAAATATGCTGATAAGTTCCAGGGA CGCTTACCTTCACTTCGGATACCTCTACCAGCACTGCCATATATGGAACCTCCGCAACCTCAAAAGT GATGACACGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGAC TACTGGGCGCAAGGCATACGGTCACCGTCTCCTCAGGTGGTGGTGTCTGCGCGCGCGGCTCC GGTGGTGGTGTCTGACATCGTGATGACACAGTCTCCAGACTCCATGACTGTGTCTCTGGCGGAG AGGACCAACCATCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCACGAATAAGAACTCCTTA GCTTGGTACAGAGAGAAAACAGGACAGCTCCTAAAATTAATCTCTCTCTGGGCATCTACGCGGAA TCCGGATCCTTGACCGATTAGTGGCAGCGGGTCTGGGACAGATTTCACTCTCACTATTGACAGC CTGACGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCACTTCCCGATCACTTTGGC CAAGGACACGACTGGACATTTAAATCCGGAGGTGGTGGCTCCGAGGTGCAGTGGTCGAGTCTGGA GGAGGATTGGTCAGCTGGAGGGTCAATTGAAACTCTCATGTGCAGCTCTGGATTCACTTCAAT AAGTACGCCATGAACCTGGGTCCCGCAGGCTCCAGGAAAGGGTTTGGAAATGGGTGCTCGCATAGA AGTAAATATAAATAATTATGCAACATATTATGCCGATTCAAGTGAAGACAGGTTCCCATCTCCAGA GATGATTCAAAAAACAACCTGCTTATCTACAAATGAACAACCTTGAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAATAGCTACATATCTTACTGGGCTTACTGGGCGCAAGGG ACTCTGGTCAACCGTCTCCTCAGGTGGTGGTGTCTTGGCGGCGGGCTCCGGTGGTGGTGTCT CAGACTGTGTGACTCAGGAACCTTCACCTACCGTATCACCTGGTGGAAACAGTCACTTGTGT GGCTCTCGACTGGGGCTGTACATCTGGCAACTACCCAAACTGGGTCCAACAAAAACCAGGTCAG GCACCCCGTGGTCTAAATAGGTGGGACTAAGTTCTCGCCCCCGGTACTCCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCTCTTA QVQLVQSGAEVKKPGEISVKVSKKASGYTFNYGMNWKQAPGQGLEWMGWINTYTGFTNYADKFKQ RVFTFTSDTSTAYMELRNILKSDDTAVYYCARWSWSGDYVYFDYWGQGTFTVTVSS
91	CD33 VH of F2	artificial	aa	NYGMN
92	CD33 HCDR1 of F2	artificial	aa	

[illegible]

103	CD33 F2 HL x H2C HL	artificial	aa	QVQLVQSGAEVKKPESVKVSCKASGYTFITNYGMNVWKQAPGQGLEWMGWINTYTGETINYADKFKQG RVFTTSDTSTSTAYMELRNILKSDDDTAVYYCARWSWSDGYVYFDYWGQGTFTVTVSSGGGGSGGGGS GGGSDIVMTQSPDLSVSLGERTTINCKSSQSLDSSSTNKNLSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGSDTDFTLTIDSLQPEDSATYCYQQSAHFPITFTGQGRLEIKSGGGGSEVQLVESG GGILVQPGGSLKLSCAAASGFTFNKYAMNVWRQAPGKGLEWVARIRSKYNNIYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNFGNSIYSWAYWGQGTILVTVSSGGGGSGGGSGGGGS QTVVTQEPSTLTVSPGGTVTLITCGSSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTRKFLAPGTPARFSG SLLGGKAALTLISGVQPEDEAEFYCVLWYSNRWVFGGGTKLTVL
104	CD33 F2 HL x H2C HL	artificial	nt	CAGGTGCAGCTGGGTGCAGTCTGGAGGTGAGGTGAAGAAAGCCTTGGAGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAAACATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGTGGATAAAACACCTACACTGGAGAGACAAAATATGCTGATAAGTTCCAGGGA CGGTACCTTCACCTTCGGATACCTCTACACGACATGCCATATATGGAACCTCCGCAACCTCAAAAGT GATGACACGGCTGTATATTTACTGTGCGCGCTGGAGTTGGAGTGTGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGGCATACGGTCACCGTCTCCTCAGGTGGTGGTTCTTGGCGGGCGGCTCC GGTGGTGGTGGTTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGTCTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCACGAATAAGAACTCCTTA GCTTGGTACCAGCAGAAAACAGGACAGCTCCTAAATTTACTCTTTCTGGGCATCTACGCGGGAA TCCGGGATCCCTGACCGATTTCAGTGGCAGCGGTCTGGGACAGATTTCACTCTCACTATTGACAGC CTGCAGCTGAAAGATTCTGCAACTTACTATTTGCAACAGTCTGCCACTTCCCGATCACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGCTCCGAGGTGCAGCTGGTTCAGTCTGGA GGAGGATTGGTGCAGCTGGAGGGTCAATTGAAAACCTCTCATGTGCAGCTCTTGATTTCACTTTCAAT AAGTACCGCATGAACTGGGTCCCGCAGGCTCCAGGAAAAGGTTTGGAAATGGGTGTCTCGCATAGA AGTAAATATAATAATATGCAACATATTTATGCCGATTTCAGTGAAGACAGGTTACCATCTCCAGA GATGATTCAAAAAACACTGCCATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACCTTCGGTAAATAGCTACATATCTTACTTGGGTACTTGGGGCCAAAGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGTCTTGGCGGCGCGGCTCCGGTGGTGGTGGTCTT CAGACTGTTGTGACTCAGGAACCTTCACCTACCGTATCACCTGGTGAACAGTCACACTCACTTGT GGCTCCTCGACTGGGGCTGTACATCTGGCTACTACCCAAACTGGGTCCAAACAAAAACAGGTCAG GCACCCCGTGGTCTAAATAGGTGGACTAAAGTTCCCTGCCCGCGGTACTCTTGCAGATTTCTCAGGC TCCCCTGCTTGGAGCAAGGCTGCCCTCACCCCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTCGGTGGAGGAACCAAACTGACTGTCTCTA
105	CD33 F2 HL x F12Q HL	artificial	aa	QVQLVQSGAEVKKPESVKVSCKASGYTFITNYGMNVWKQAPGQGLEWMGWINTYTGETINYADKFKQG RVFTTSDTSTSTAYMELRNILKSDDDTAVYYCARWSWSDGYVYFDYWGQGTFTVTVSSGGGGSGGGGS GGGSDIVMTQSPDLSVSLGERTTINCKSSQSLDSSSTNKNLSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGSDTDFTLTIDSLQPEDSATYCYQQSAHFPITFTGQGRLEIKSGGGGSEVQLVESG GGILVQPGGSLKLSCAAASGFTFNKYAMNVWRQAPGKGLEWVARIRSKYNNIYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNFGNSIYSWAYWGQGTILVTVSSGGGGSGGGSGGGGS QTVVTQEPSTLTVSPGGTVTLITCGSSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTRKFLAPGTPARFSG SLLGGKAALTLISGVQPEDEAEFYCVLWYSNRWVFGGGTKLTVL

106	CD33 F2 HL x F12Q HL	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAACTATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGACAAACTATGCTGATAAGTTCCAGGGA CGCGTTACCTTCACCTTCGGATACCTCTACCAGCACTGCCATATATGGAACCTCCGCAACCTCAAAAGT GATGACACGGCTGTATATTAATGCTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCAAGGCATACGGTCACCGTCTCCTCAGGTGGTGGTGGTCTGGCGCGCGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGTCTGTGTCTCTGGCGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCACGAATAAGAACTCCTTTA GCTTGGTACACAGAGAAAACAGGACAGCTCCTAAAATTACTCTCTTCTGGGCATCTACGCGGAA TCCGGATCCTTGACCGATTAGTGGCAGCGGCTCTGGGACAGATTACTCTACTATATGACAGC CTGACGCTGAAAGATTCTGCAACTTACTATTTGTCACAGCTTGCCCACTTCCCGATCACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGTGGTCGAGTCTGGA GGAGGATTGGTGCAGCTGGAGGGTCAATTGAAACTCTCATGTGAGCCTCTGGATTCACTTCAAT AGCTACGCCATGAACTGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAAATGGTGTGCTCGCATAGA AGTAAATATAAATAATTATGCAACATATATGCCGATTGAGTGAAGGAGGTTTCCATCTCCAGA GATGATTCAAAAACACTGCCTATCTACAAATGAACAACTTGAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGAACTTCGGTAATAGCTACGTTTCTGGTGGCTTACTGGGGCAAGGG ACTCTGGTCAACCGTCTCCTCAGGTGGTGGTCTTGGCGCGCGGCTCCGGTGGTGGTCTT CAGACTGTTGTGACTCAGGAACTTCACCTACCGTATACCTGGTGGAAACAGTCACACTCACTTGT GGCTCTCGACTGGGCTGTACATCTGGCAACTACCCAACTGGGTCCAAACAAACACAGGTGAG GCACCCGTGGTCTAATAGGTGGGACTAAGTTCTTCCGCCCCGCTACTCTTCCAGATTCTCAGGC TCCCCTGTTGGAGGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGACAGAAATAT TACTGTGTTCTATGTTACAGCAACCGTGGGTGTTCTGGTGGAGAAACCAACTGACTGTCTCTA
107	CD33 F2 HL x I2C HL	artificial	aa	QVQLVQSGAEVKKPESVKVSKASGYTFTNYGMWVYKQAPGQGLEWMGWINTYTGENTYADKFKQ RVFTSDTSTSTAYMELRNLIKSDDTAVYYCARWSWDGYVYFDYWGQGTFTVTVSSGGGSGGGGS GGGSDIVMTQSPDSLVSLEGERTTINCKSSQSLDSTNKNLSLAWYQQKPKPQLILLISWASTRE SGIPDRFSGSGSDTFTLTIDSLQPEDSATYCYQQSAHFPITFGQGTREIKSGGGGSEVQLVESG GGIVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNIATYADSVKDRFTISR DDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISWAYWGQGTFTVTVSSGGGSGGGGSGGGGS QTVVTQEPSTLTVSPGGFTVLTLCGSSTGAVTSGNYPNWYQKPKQAPRGLIGGTFKLAPGTPARFSG SLLGGKAALTLISGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL
108	CD33 F2 HL x I2C HL	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAACTATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGACAAACTATGCTGATAAGTTCCAGGGA CGCGTTACCTTCACCTTCGGATACCTCTACCAGCACTGCCATATATGGAACCTCCGCAACCTCAAAAGT GATGACACGGCTGTATATTAATGCTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGAC TACTGGGGCAAGGCATACGGTCACCGTCTCCTCAGGTGGTGGTGGTCTGGCGCGCGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGTCTGTGTCTCTGGCGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCACGAATAAGAACTCCTTTA

				GCTTGGTACCAGCAGAAAAACAGGACAGCCTCCTAAATTAATCTCTCTTCTGGGCATCTACGCGGAA TCCGGGATCCCTGACCGATTTCAGTGGCAGCGGTCTGGGACAGATTCTACTCTCTACTATTGACAGC CTGCAGCCTGAAAGATTCTGCAACTTACTATTGTCAACAGCTTGCCCACTTCCCGATCACCTTTGGC CAAGGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGCTGGTCGAGTCTGGA GGAGGATTGGTCAGCCTGGAGGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAAT AAGTACGCCATGAATGGGTCCGCGAGGCTCCAGGAAAGGGTTTGAATGGGTGCTCGCATAGA AGTAAATATAATAATATGCAACATATATGCCGATTTCAGTGAAGACAGGTTACCATCTCCAGA GATGATCAAAAAAACACTGCTTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGACAGACATGGGAACTTCCGTTAATAGCTACATATCTCTACTGGGTCTACTGGGGCCAAGGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGTCTTGCGGGCGGGCTCCGGTGGTGGTGTCT CAGACTGTTGTGACTCAGGAACTTCACTCACCGTATCACCTGGTGGAAACAGTCACACTCACTTGT GGCTCCTCGACTGGGGCTGTTACATCTGGCAACTACCCAACTGGGTCCAAACAAAAACAGGTCTAG GCACCCCGTGGTCTAAATAGGTGGGACTAAAGTTCTCTGCCCCGGTACTCCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGTTCTATGGTACAGCAACCGCTGGGTGTTCTCGTGAGGAAACCAAACTGACTGTCTCTA QVQLVQSGAEVKKPGESVKVSKASGYTFINYGMMWVKQAPGQGLEWMGWINTYTGEPTYADKFGG RVMTDTSTSTAYMEIRNLRSDDTAVYYCARWSWSDDGYVYFDYWGQGTTVTVSS
109	CD33 VH of B10	artificial	aa	NYGMN
110	CD33 HCDR1 of B10	Artificial	aa	WINTYTGEPTYADKFGG
111	CD33HCDR2 of B10	artificial	aa	WSWSDGYVYFDY
112	CD33 HCDR3 of B10	artificial	aa	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGTGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCCAACTATGCTGATAAGTTCAGGGA CGCGTTACCATGACTACGGATACCTCTACCAGCACTGCCTATATGGAATCCGCAACCTCAGAAAT GATGACACGCGCTATATTAATGTCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGCGCAAGGCACACTACGGTCACCGTCTCCTCA
113	CD33 VH of B10	artificial	nt	DIVMTQSPDLSLTSLGERTTINCKSSQSVLDSNNKNSLAWYQQKPGQPPKLLLSWASTRESGIPD RFGSGSGTDFTLTIDGLQPEDSATYFCQQSAHFPIITFGQGTRLFIEIK
114	CD33 VL of B10	artificial	aa	KSSQSVLDSNNKNSLA
115	CD33 LCDR1 of B10	artificial	aa	WASTRES
116	CD33 LCDR2 of B10	artificial	aa	QQSAHFPIIT
117	CD33 LCDR3 of B10	artificial	aa	GACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTTGGGCGAGAGGACCACCATCAAC
118	CD33 VL of B10	artificial	nt	

119	CD33 HL of B10	artificial	aa	TGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAACAATAAGAACTCCTTAGCTTGGTACCAGCAG AAAACGAGACAGCCTCCTAAATTTACTCCTTTCTGGGCATCTACGCGGGAATCCGGGATCCCTTGAC CGATTCAAGTGGCAGCGGTCTTGGGACAGATTTCACTCTCACTATTGACGCGCTGCAGCCTGAAGAT TCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCAGTACCTTTGGCCAAAGGACACAGACTG GAGATTAAA QVQLVQSGAEVKKPGEISVKVSKKASGYTFITNYGMNWKQAPGQGLEWMGWINTYTGEPYADKFFQG RVMTTDTSTSTAYMEIRNLRSDDTAVYICARWSWSDGYVYFDYWGQGTFTVTVSSGGGSGGGGS GGGGDIVMTQSPDLSLTIVSLGERITINCKSSQSLDSSNNKNSLAWYQOKPGQPPKLLLSWASTRE SGIPDRFSGSGGTDFLTITDGLQPEDSATYFCQSSAHFPIITFGQGTRLEIK CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGTGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAAATATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGTGGATAAAACACTACACTGAGAGAGCAACCTATGCTGATAAGTTCCAGGGA CGGTACCATGACTACGGATACCTCTACCAGACTGCCATATATGGAATCCGCAACCTCAGAAAT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTACTTTTAC TACTGGGGCCAAAGGACTACGGTCACCGTCTCCTCAGGTGGTGGTTCTTGGCGGCGGCTCC GGTGGTGGTGGTTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAACAATAAGAACTCCTTA GCTTGTACACAGAGAAACAGGACAGCTCCTAAATTTACTCCTTTCTGGGCATCTACGCGGGAA TCCGGGATCCCTGACCGATTCAAGTGGCAGCGGTCTTGGGACAGATTTCACTCTCACTATTGACGGC CTGCAGCCTGAAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCAGTCACTTTTGGC CAAGGACACGACTGGAGATTAAA
120	CD33 HL of B10	artificial	nt	QVQLVQSGAEVKKPGEISVKVSKKASGYTFITNYGMNWKQAPGQGLEWMGWINTYTGEPYADKFFQG RVMTTDTSTSTAYMEIRNLRSDDTAVYICARWSWSDGYVYFDYWGQGTFTVTVSSGGGSGGGGS GGGGDIVMTQSPDLSLTIVSLGERITINCKSSQSLDSSNNKNSLAWYQOKPGQPPKLLLSWASTRE SGIPDRFSGSGGTDFLTITDGLQPEDSATYFCQSSAHFPIITFGQGTRLEIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAASGFTFNKYAMNWKQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYICVRHGNFNSYISYWAYWGQGTFTVTVSSGGGSGGGGSGGGGS QTAVTQEPSTLTVSPGGTFTLTITCGSSTGAVTSGYYPNWKQAPGQAPRGLIGGTFKFLAPGTPARFSG SLLGGKAAALTLISGVQPEDEAEFYCALWYSNRWVFGGGTKLITVL CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGTGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAAATATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGTGGATAAAACACTACACTGAGAGAGCAACCTATGCTGATAAGTTCCAGGGA CGGTACCATGACTACGGATACCTCTACCAGACTGCCATATATGGAATCCGCAACCTCAGAAAT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTACTTTTAC TACTGGGGCCAAAGGACTACGGTCACCGTCTCCTCAGGTGGTGGTTCTTGGCGGCGGCTCC GGTGGTGGTGGTTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAACAATAAGAACTCCTTA GCTTGTACACAGAGAAACAGGACAGCTCCTAAATTTACTCCTTTCTGGGCATCTACGCGGGAA TCCGGGATCCCTGACCGATTCAAGTGGCAGCGGTCTTGGGACAGATTTCACTCTCACTATTGACGGC
121	CD33 B10 HL x H2C HL	artificial	aa	QVQLVQSGAEVKKPGEISVKVSKKASGYTFITNYGMNWKQAPGQGLEWMGWINTYTGEPYADKFFQG RVMTTDTSTSTAYMEIRNLRSDDTAVYICARWSWSDGYVYFDYWGQGTFTVTVSSGGGSGGGGS GGGGDIVMTQSPDLSLTIVSLGERITINCKSSQSLDSSNNKNSLAWYQOKPGQPPKLLLSWASTRE SGIPDRFSGSGGTDFLTITDGLQPEDSATYFCQSSAHFPIITFGQGTRLEIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAASGFTFNKYAMNWKQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYICVRHGNFNSYISYWAYWGQGTFTVTVSSGGGSGGGGSGGGGS QTAVTQEPSTLTVSPGGTFTLTITCGSSTGAVTSGYYPNWKQAPGQAPRGLIGGTFKFLAPGTPARFSG SLLGGKAAALTLISGVQPEDEAEFYCALWYSNRWVFGGGTKLITVL CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGTGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAAATATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGTGGATAAAACACTACACTGAGAGAGCAACCTATGCTGATAAGTTCCAGGGA CGGTACCATGACTACGGATACCTCTACCAGACTGCCATATATGGAATCCGCAACCTCAGAAAT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTACTTTTAC TACTGGGGCCAAAGGACTACGGTCACCGTCTCCTCAGGTGGTGGTTCTTGGCGGCGGCTCC GGTGGTGGTGGTTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAACAATAAGAACTCCTTA GCTTGTACACAGAGAAACAGGACAGCTCCTAAATTTACTCCTTTCTGGGCATCTACGCGGGAA TCCGGGATCCCTGACCGATTCAAGTGGCAGCGGTCTTGGGACAGATTTCACTCTCACTATTGACGGC
122	CD33 B10 HL x H2C HL	artificial	nt	QVQLVQSGAEVKKPGEISVKVSKKASGYTFITNYGMNWKQAPGQGLEWMGWINTYTGEPYADKFFQG RVMTTDTSTSTAYMEIRNLRSDDTAVYICARWSWSDGYVYFDYWGQGTFTVTVSSGGGSGGGGS GGGGDIVMTQSPDLSLTIVSLGERITINCKSSQSLDSSNNKNSLAWYQOKPGQPPKLLLSWASTRE SGIPDRFSGSGGTDFLTITDGLQPEDSATYFCQSSAHFPIITFGQGTRLEIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAASGFTFNKYAMNWKQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYICVRHGNFNSYISYWAYWGQGTFTVTVSSGGGSGGGGSGGGGS QTAVTQEPSTLTVSPGGTFTLTITCGSSTGAVTSGYYPNWKQAPGQAPRGLIGGTFKFLAPGTPARFSG SLLGGKAAALTLISGVQPEDEAEFYCALWYSNRWVFGGGTKLITVL CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGTGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAAATATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGTGGATAAAACACTACACTGAGAGAGCAACCTATGCTGATAAGTTCCAGGGA CGGTACCATGACTACGGATACCTCTACCAGACTGCCATATATGGAATCCGCAACCTCAGAAAT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTACTTTTAC TACTGGGGCCAAAGGACTACGGTCACCGTCTCCTCAGGTGGTGGTTCTTGGCGGCGGCTCC GGTGGTGGTGGTTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAACAATAAGAACTCCTTA GCTTGTACACAGAGAAACAGGACAGCTCCTAAATTTACTCCTTTCTGGGCATCTACGCGGGAA TCCGGGATCCCTGACCGATTCAAGTGGCAGCGGTCTTGGGACAGATTTCACTCTCACTATTGACGGC

123	CD33 B10 HL x F12Q HL	artificial	aa	CTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACACTTCCCAGATCACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGTGGTCGAGTCTGGA GGAGGATTGGTGCAGCCTGGAGGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAAT AAGTACGCCATGAACCTGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAAATGGGTGCTCGCATAGA AGTAAATATAAATAATTATGCAACATATTATGCCGATTAGTGAAGACAGGTTACCATCTCCAGA GATGATTCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAATAGTACATATCTTACTGGGTACTTGGGGCCAAGGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGGTCTTGGCGCGCGCGGTCCCGGTGGTGGTCTCT CAGACTGTTGTGACTCAGGAACCTTCACCTACCGTATACCTGGTGGAAACAGTCACTTCTGT GGCTCTCGACTGGGGCTGTACATCTGGCTACTACCCAAACTGGGTCCAACAAAAACAGGTTCAG GCACCCCGTGGTCTAAATAGGTGGACTAAGTTCTTCCGCCCGGTACTCTTCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTCTGGTGGAGGAACCAAACTGACTGTCTCTA QVQLVQSGAEVKKPGESVKVSKKASGYTFITNYGMNWVKQAPQGLEWMGWINTYITGEPTYADKFQG RVITMTDTSTSTAYMEIRNLRSDDTAVYICARWSWSDGYVYFDYWGQGTITVTVSSGGGSGGGGS GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSNNKNSLAWYQKPGQPPKLLLSWASTRE SGIPDRFSGSGSDFTLTIDGLQPEDSATYCYQQSAHFPITFTGQGRLEIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKNNIYATYADSVKGRFTISR DDSKNTAYLQMNNLKTEDTAVYICVRHGNFNSYVSWWAYWGQTLITVSSGGGSGGGGSGGGGS QTVVTEPSLTVSPGGFVTLTTCGSSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTGKLTIVL
124	CD33 B10 HL x F12Q HL	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGTGAGTCAGTCAAGGTCTCTCTGC AAGGTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGTGGATAAAACACCTACACTGGAGAGCCAACTATGCTGATAAGTTCAGGGA CGCGTTACCATGACTACGGATACCTCTACCAGCACTGCCATATATGGAATCCGCAACCTCAGAAAT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGAC TACTGGGGCCAAAGCACTACGGTCACCGTCTCCTCAGGTGGTGGTGGTCTTGGCGCGCGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCAAACAATAAGAACTCCCTTA GCTTGTGTACAGAGAAAACAGGACAGCTCCCTAAATTACTCCTTCTTGGGCATCTACGCGGAA TCCGGGATCCCCTGACCCGATTTCAGTGGCAGCGGTCTTGGGACAGATTTCAC'TCTCAC'TATTGACGGC CTGCAGCCTGAAGATTCTTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCAGATCACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGCTCCGAGGTGACGTGGTTCGAGTCTGGA GGAGGATTGGTGCAGCTGGAGGGTCAATTGAAACTCTCATGTGCAGCTCTGGATTCACTTCAAT AGCTACGCCATGAACCTGGGTCCGCCAGGCTCCAGGAAAAGGTTTGGAAATGGGTGCTCGCATAGA AGTAAATATAAATAATTATGCAACATATTATGCCGATTTCAGTGAAGAGCAGGTTACCATCTCCAGA GATGATTCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAATAGTACGTTTCTTGGTGGGCTTACTTGGGGCCAAGGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGGTCTTGGCGCGCGGCTCCGGTGGTGGTGGTCTCT

125	CD33 B10 HL x I2C HL	artificial	aa	CAGACTGTTGTGACTCAGGAACCTTCACCTCACCGTATACCTGGTGGAACAGTCACACTCACTTGT GGCTCCTCGACTGGGGCTGTTACATCTGGCAACTACCCAAACTGGGTCCAAACAAAAACAGGTTCAG GCACCCCGTGGTCTAAATAGGTGGGACTAAGTTCCTCGCCCCCGGTACTCCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAATAT TACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTTCGGTGAGGAACCAAACTGACTGTCTCTA QVQLVQSGAEVKKPGEISVKVSCKASGYTFITNYGMNWKQAPGQGLEWMGWINTYTGEPYADKFFQG RVMTTDTSTSTAYMEIRNLRSDDTAVYYCARWSWSDGYVYFDYWGQGTFTVTVSSGGGSGGGGS GGGGDIVMTQSPDSLTVSLGERFTINCKSSQSLDSSNNKNSLAWYQOKPGQPPKLLLSWASTRE SGIPDRFSGSGSGTDFTLTIDGLQPEDSATYFCQOQSAHFPITFGQGTRLFIKSGGGGSEVQLVIESG GGLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKGLIEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGLVTVSSGGGSGGGGSGGGGS QTVVTEPESLTVSPGGTVTLTTCGSSTGAVTSGNYPNWVQOKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGKKAALTLSGVQPEDEAEYYCYLWYSNRWYFGGGTKLTVL
126	CD33 B10 HL x I2C HL	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAGCCTGGTGAGTCAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGGTATACCTTCACAAACTATGGAAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCAACCTATGCTGATAAAGTTCAGGGGA CGGTTACCATGACTACGGATACCTTACCAGCACTGCCATATATGGAATCCGCAACCTCAGAAAT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGAC TACTGGGGCCAAAGGCATACGGTCACCGTCTCCTCAGGTGGTGGTGTCTGGCGGCGGGCTCC GGTGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCCTGACTGTGTCTCTGGGCGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAACAATAAGAACTCCTTTA GCTTGTACACAGCAGAAAAACAGGACAGCTCCTAAAATTACTCTCTTCTCTGGGCATCTACGCGGAA TCCGGGATCCCTGACCGATTTCAGTGGCAGCGGTTCTGGGACAGATTTCATCTCCTACTATTGACGGC CTGCAGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCCACTTCCCGATCACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGTGGTCGAGTCTGGA GGAGGATTGGTGCAGCTGGAGGGTCATTGAAACTCTCATGTGCAGCTCTGGATTCACTTCAAT AAGTACGCCATGAACCTGGGTCCGCCAGGCTCCAGGAAAGGTTTGGAAATGGGTGCTCGCATAGA AGTAAATATAAATATGCAACATATTATGCCGATTTCAGTGAAGACAGGTTCCCATCTCCAGA GATGATTCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAAATAGCTACATATCTTACTGGGCTTACTGGGGCCAAGGG ACTCTGGTCAACCGTCTCCTCAGTGGTGGTGGTTCCTGGCGGCGGGCTCCGGTGGTGGTGGTCT CAGACTGTTGTGACTCAGGAACCTTCACTACCGTATACCTGGTGGAACAGTCACACTCACTTGT GGCTCCTCGACTGGGGCTGTACATCTGGCAACTACCCAAACTGGGTCCAAACAAAAACAGGTTCAG GCACCCCGTGGTCTAAATAGGTGGGACTAAGTTCCTCGCCCCCGGTACTCCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAATAT TACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTTCGGTGAGGAACCAAACTGACTGTCTCTA
127	CD33 VH of E11	artificial	aa	QVQLVQSGAEVKKPGEISVKVSCKASGYTFITNYGMNWKQAPGQGLEWMGWINTYTGEPYADKFFQG RVMTTDTSTSTAYMEIRNLGDDDTAVYYCARWSWSDGYVYFDYWGQGTFTVTVSS

128	CD33 HCDR1 of E11	artificial	aa	NYGMN	
129	CD33 HCDR2 of E11	artificial	aa	WINTYTGEPTYADKFGQ	
130	CD33 HCDR3 of E11	artificial	aa	WSWSDGYVYVFDY	
131	CD33 VH of E11	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAACCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAACTATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAACACCTACACTGGAGAGCCAACTATGCTGATAAGTTCCAGGGA CGCGTTACCATGACTACGGATACCTCTACCAGCACTGCCTATATGGAATCCGCAACCTCGGAGGT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGCACTTCGGTCACCGTCTCCTCA	
132	CD33 VL of E11	artificial	aa	DIVMTQSPDLSLTIVSLGERTTINCKSSQSVLDSSTNKNLSLAWYQQKPGQPPPKLLLSWASTRESGIPD RFGSGSGGTDFTLTIDSPQPEDSATYCYQQSAHFPIITFGQGRLEIK	
133	CD33 LCDR1 of E11	artificial	aa	KSSQSVLDSSTNKNLSLA	
134	CD33 LCDR2 of E11	artificial	aa	WASTRES	
135	CD33 LCDR3 of E11	artificial	aa	QQSAHFPIIT	
136	CD33 VL of E11	artificial	nt	GACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGACCAACATCAAC TGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCACGAAATAAGAACTCCTTAGCTTGGTACCAGCAG AAACCAGGACAGCCTCCTAAATTACTCCTTCTCGGGCATCTACGCGGGAATCCGGGATCCCTGAC CGATTCAGTGGCAGCGGGTCTGGGACAGATTTCACTCTCACTATTGACAGCCCGCAGCCTGAAGAT TCTGCAACTTACTATTGTCAACAGTCTGCCCACTTCCCAGATCACCTTTGGCCCAAGGACACGACTG GAGATTAAA	
137	CD33 HL of E11	artificial	aa	QVQLVQSGAEVKKPGEISVKVSKKASGYTFITNYGMNWVKQAPGQGLEWMGWINTYTGEPTYADKFGQ RVTMTTDTSTSTAYMEIRNLGGDDTAVYICARWSWSDGYVYVFDYWGQGTSTVTVSSGGGSGGGGS GGGSDIVMTQSPDLSLTIVSLGERTTINCKSSQSVLDSSTNKNLSLAWYQQKPGQPPPKLLLSWASTRE SGIPDRFSGSGGTDFTLTIDSPQPEDSATYCYQQSAHFPIITFGQGRLEIK	
138	CD33 HL of E11	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAACCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGCTAGCGGGTATACCTTCACAAACTATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAACACCTACACTGGAGAGCCAACTATGCTGATAAGTTCCAGGGA CGCGTTACCATGACTACGGATACCTCTACCAGCACTGCCTATATGGAATCCGCAACCTCGGAGGT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGCACTTCGGTCACCGTCTCCTCAGGTGGTGGTTCCTGAGTGTCTTCTGGCGGCGGCTCC GGTGGTGGTGTCTTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCACGAATAAGAACTCCTTA	

139	CD33 E11 HL x H2C HL	artificial	aa	GCTTGGTACCAGCAGAAAACAGGACAGCCTCCTAAATTACTCCTTTCTTGGCATCTACGCGGGAA TCCGGGATCCCTGACCGATTCACTGGCAGCGGCTCTGGGACAGATTCTACTCTCACTATTGACAGC CCGAGCCTGAAAGATTCTGCAACTTACTATTGTCAACAGCTCTGCCCACTTCCCGATCACTTTCGCG CAAGGACACGACTGGAGATTAAA QVQLVQSGAEVKKPGEISVKVSKKASGYTFITNYGMNWVKQAPGQGLEWMGWINTYTGEPYADKFFQG RVITMTDTSTSTAYMEIRNLGGDDTAVYICARWSWSDGYVYFDYWGQGTSTVTVSSGGGGSGGGGS GGGSDIVMTQSPDLSLTSLGERTTINCKSSQSLDSTNKNLSLAWYQKPKGPPKILLISWASTRE SGIPDRFSGSGSDTFTLTIDSPQEDSATYCYQQSAHFPITFGQGRLEIKSGGGGSEVQLVESG GGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLIEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTLLVTVSSGGGGSGGGSGGGGS QTVVTEPSLTVSPGGTVTLTTCGSSTGAVTSGYYPNWVQKPKGAPRGLIGGTFKLAPGTPARFSG SLLGKKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
140	CD33 E11 HL x H2C HL	artificial	nt	CAGGTGACGCTGGTGACGCTGGAGCTGAGGTGAAGAAGCCTGGAGAGTCAGTCAAGGTCTCCTGTC AAGGCTAGCGGGTATACCTTTCACAAAATATGGAAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGTGGATAAACACCTACACTGGAGAGCAACCTATGCTGATAAGTTCCAGGGA CGCTTACCATGACTACGGATACCTCTACCAGCACTGCCATATATGGAATCCGCAACCTCGAGGT GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGAC TACTGGGGCAAGGCACCTTCGGTCACCGCTCCTCAGGTGGTGGTGTCTGCGCGCGCGGCTCC GGTGGTGGTGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCAACATCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCACGAATAAGAACTCCTTA GCTTGGTACCAGCAGAAAACAGGACAGCCTCCTAAAATTACTCTCTTCTTGGGCATCTACGCGGAA TCCGGATCCTTGACCGATTCACTGGCAGCGGCTCTGGGACAGATTCTACTCTCACTATTGACAGC CCGAGCCTGAAAGATTCTGCAACTTACTATTGTCAACAGCTTGCCCACTTCCCGATCACTTTGGC CAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGCTCCGAGGTGCAGTGGTCGAGTCTGGA GGAGGATTGGTCAGCCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAAT AAGTACGCCATGAACCTGGGTCCCGCAGGCTCCAGGAAAGGGTTTGGAAATGGGTGCTCGCATAGA AGTAAATATAAATAATTATGCAACATATTATGCCGATTCACTGAAAGACAGGTTCAACATCTCCAGA GATGATTCAAAAAACACTGCCATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAATAGCTACATATCCTACTGGGTACTTGGGGCAAGGG ACTCTGGTCAACCGTCTCCTCAGGTGGTGGTGTCTTGGCGGCGGCTCCGGTGGTGGTGTCT CAGACTGTGTGACTCAGGAACTTCACTACCGTATCACTGGTGGAAACAGTCACTCACTTGT GGCTCTCGACTGGGGCTGTACATCTGGCTACTACCCAACTGGGTCCAACAAAAACAGGTCAAG GCACCCCGTGTCTAATAGGTGGGACTAAGTTCTGCCCCCGGTACTCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGTGCCCTCACCTCTCAGGGTACAGCCAGGATGAGGCAGAGATAAT TACTGTGCTCTATGTTACAGCAACCGTGGGTGTTCGGTGGAGGAAACCAACTGACTGTCTTA
141	CD33 E11 HL x F12Q HL	artificial	aa	QVQLVQSGAEVKKPGEISVKVSKKASGYTFITNYGMNWVKQAPGQGLEWMGWINTYTGEPYADKFFQG RVITMTDTSTSTAYMEIRNLGGDDTAVYICARWSWSDGYVYFDYWGQGTSTVTVSSGGGGSGGGGS GGGSDIVMTQSPDLSLTSLGERTTINCKSSQSLDSTNKNLSLAWYQKPKGPPKILLISWASTRE SGIPDRFSGSGSDTFTLTIDSPQEDSATYCYQQSAHFPITFGQGRLEIKSGGGGSEVQLVESG

142	CD33 E11 HL x F12Q HL	artificial	nt	GGLVQPGGSLKLSCAAAGFTFNSYAMNWWVQAPGKGLEWVARIRSKYNNIYATYYADSVKGRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNFNSYVSWWAYWQGTLVTVSSGGGSGGGSGGGGS QTVVTTQEPSTLVSPGGTVTLTCSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAAALTLISGVQPEDEAFYYCVLWYSNRWVFGGGTKLTVL CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAACTATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCAACCTATGCTGATAAGTTCAGGGA CGGTTACCATGACTACGGATACCTCTACAGCACTGCCTATATGAAATCCGCAACCTCGGAGGT GATGACACGGCTGTATATTAATGTGCGCGTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCAAGGCACCTTCGGTCACCGTCTCTCAGGTGGTGGTGGTTCTTGGCGGCGGGCTCC GGTGGTGGTGGTCTGACATCGTAGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACTCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCACGAAATAAGAACTCCTTA GCTTGGTACCAGAGAAAACAGGACAGCTCCTAAATTAATTAATTAATTAATTAATTAATTAATTA TCCGGGATCCCTGACCGATTGAGTGGCAGCGGTCTGGGACAGATTCTACTTCTACTATTGACAGC CCGAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCCACTTCCCGATCACCCTTGGC CAAGGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGCTCTGGATTCACTTCAAT GGAGGATTGGTGCAGCTGGAGGTCAATTGAAACTCTCATGTGCAGCTCTGGATTCACTTCAAT AGCTACGCCATGAATGGGTCCCGCAGGCTCCAGGAAAGGTTTGGAAATGGTGGTCTCGCATAAAGA AGTAAATATAATAATATGCAACATATATGCGGATTGAGTGAAGGAGGTTTCAACATCTCCAGA GATGATCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACTTCGGTAATAGCTACGTTTCTTGGTGGCTTACTTGGGCGCAAGGG ACTCTGGTCACCGTCTCTCAGGTGGTGGTGGTCTTGGCGGCGGGCTCCGGTGGTGGTGGTCTT CAGACTGTGTGACTCAGGAACTTCACCTACCGTATCACTGGTGGAAACAGTCACTCACTTGT GGCTCCTCGACTGGGGCTGTTACATCTGGCAACTACCCAACTGGGTCCAAACAAACCCAGGTGAG GCACCCCGTGGTCTAAATAGGTGGGACTAAGTTCTTCCGCCCCGGTACTCTCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGGATGAGGCAGAAATAT TACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTCTGGTGGAGGAACCAACTGACTGTCTCTA QVQLVQSGAEVKKPGEISVKVSCKASGYTFITNYGMNWKQAPGQGLEWMGWINTYTGEPTIYADKFFQG RVTMTTDTSTSTAYMEIRNLGGDDTAVYYCARWSWSDGYVYFDYWGQGTSTVTVSSGGGSGGGGS GGGSDIVMTQSPDSTLVSLGERITINCKSSQSVLDSSTNKNLSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGGTDFLTIDSPQPEDSATYCYQOQSAHFPITFGQGTRLIEIKSGGGGSEVQLVIESG GGLVQPGGSLKLSCAAAGFTFNSYAMNWWVQAPGKGLEWVARIRSKYNNIYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNFNSYISYWAYWQGTLVTVSSGGGSGGGSGGGGS QTVVTTQEPSTLVSPGGTVTLTCSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAAALTLISGVQPEDEAFYYCVLWYSNRWVFGGGTKLTVL CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAACTATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCAACCTATGCTGATAAGTTCAGGGA CGGTTACCATGACTACGGATACCTCTACAGCACTGCCTATATGAAATCCGCAACCTCGGAGGT
143	CD33 E11 HL x I2C HL	artificial	aa	QVQLVQSGAEVKKPGEISVKVSCKASGYTFITNYGMNWKQAPGQGLEWMGWINTYTGEPTIYADKFFQG RVTMTTDTSTSTAYMEIRNLGGDDTAVYYCARWSWSDGYVYFDYWGQGTSTVTVSSGGGSGGGGS GGGSDIVMTQSPDSTLVSLGERITINCKSSQSVLDSSTNKNLSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGGTDFLTIDSPQPEDSATYCYQOQSAHFPITFGQGTRLIEIKSGGGGSEVQLVIESG GGLVQPGGSLKLSCAAAGFTFNSYAMNWWVQAPGKGLEWVARIRSKYNNIYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNFNSYISYWAYWQGTLVTVSSGGGSGGGSGGGGS QTVVTTQEPSTLVSPGGTVTLTCSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAAALTLISGVQPEDEAFYYCVLWYSNRWVFGGGTKLTVL CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAACTATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCAACCTATGCTGATAAGTTCAGGGA CGGTTACCATGACTACGGATACCTCTACAGCACTGCCTATATGAAATCCGCAACCTCGGAGGT
144	CD33 E11 HL x I2C HL	artificial	nt	QVQLVQSGAEVKKPGEISVKVSCKASGYTFITNYGMNWKQAPGQGLEWMGWINTYTGEPTIYADKFFQG RVTMTTDTSTSTAYMEIRNLGGDDTAVYYCARWSWSDGYVYFDYWGQGTSTVTVSSGGGSGGGGS GGGSDIVMTQSPDSTLVSLGERITINCKSSQSVLDSSTNKNLSLAWYQQKPGQPPKLLLSWASTRE SGIPDRFSGSGGTDFLTIDSPQPEDSATYCYQOQSAHFPITFGQGTRLIEIKSGGGGSEVQLVIESG GGLVQPGGSLKLSCAAAGFTFNSYAMNWWVQAPGKGLEWVARIRSKYNNIYATYYADSVKDRFTISR DDSKNTAYLQMNILKTEDTAVYYCVRHGNFNSYISYWAYWQGTLVTVSSGGGSGGGSGGGGS QTVVTTQEPSTLVSPGGTVTLTCSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAAALTLISGVQPEDEAFYYCVLWYSNRWVFGGGTKLTVL CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGC AAGGTAGCGGGTATACCTTCACAAACTATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCAACCTATGCTGATAAGTTCAGGGA CGGTTACCATGACTACGGATACCTCTACAGCACTGCCTATATGAAATCCGCAACCTCGGAGGT

145	CD33	human	nt	GATGACACGGCTGTATATTACTGTGCGCGCTGGAGTTGGAGTTGATGTTACTACGTTTACTTTTGAC TACTGGGGCCCAAGGCACTTTCGGTCACCGTCTCCCTCAGGTGGTGGTGGTTCGGCGCGCGGGCTCC GGTGGTGGTGGTTC TGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCACGAATAAGAACTCCTTTA GCTTGGTACCAGAGAAACCAGGACAGCTCTCTAAATTACTCTCTTCTCTGGGCATCTACGCGGAA TCCGGGATCCCTGACCGATTCACTGGCAGCGGGTCTGGGACAGATTTCACTCTCACTATTGACAGC CCGAGCTTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCAGTACCTTTGGC CAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGTCCGAGGTGAGTGGTGGTGGTCTGGGA GGAGGATTGGTGCAGCTGGAGGTCAATGAAACTCTCATGTGCAGCTCTGGATTCACTTCACTTCAAT AAGTACGCCATGAACTGGGTCCGCCAGGCTCCAGGAAAGGTTTGGAAATGGGTTCGTCGATAAGA AGTAAATATAATAATTATGCAACATATTATGCCGATTCACTGAGGAAAGGTTTGGAAATGGGTTCGTCGATAAGA GATGATTCAAAAAACACTGCCCTATCTACAAATGAACAACTTGAATACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACCTTCGGTAATAGCTACATATCTACTGGGCTTACTGGGSCCAAGGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGGTTCGGCGCGCGCGCTCCGGTGGTGGTGGTTCCT CAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACTGGTGGAAACAGTCACTCACTTGT GGCTCCTCGACTGGGCTGTTTACATCTGGCAACTACCCAAACTGGGTCCAAACAAAAACAGGTCAG GCACCCCGTGGTCTAAATAGGTGGGACTAAAGTTCTCGCCCCGGTACTCTGCGAGATTCTCAAGGC TCCCTGCTTGGAGGCAAGGCTGCCCCTCACCCCTCTCAGGGGTACAGGCAGAGGATGAGGACAGAAATAT TACTGTGTTCTATGGTTACAGCAACCGCTGGGTGTTTCGGTGGAGGAAACCAAACTGACTGTCTCTA ATGGGATGGAGCTGTATCATCTCTTCTTGGTAGCAACAGCTACAGGTGTACACTTCGATCCAAAT TCTTGGCTGCAAGTGCAGGAGTCAGTGACGGTACAGGAGGTTTGTGGCTCTCGTGCCTTGCACT TCTTCCATCCCATACCTTACTACGACAAAGAACTCCCACTTCTGTTACTGGTTCGCGGAAAGGA GCCATTATATCCGGGACTCTCCAGTGGCCCAACAAAGCTAGATCAAGAAAGTACAGAGAGACT CAGGCAGATTCCGCTCTTGGGGATCCAGTAGGAAACAACTGCTCCTTGAGCATCTGTAGACGCC AGGAGGAGGATAAATGGTTCACTTCTTTCGGTAGGAGAGGAAATACCAAAATACAGTTACAAA TCTCCCCAGCTCTCTGTGCATGTGACAGACTTGACCCACAGAGGCCCCAAAATCTCATCTCCCTGGCACT CTAGAACCCGGCCACTCCAAAAACCTGACCTGCTCTGTGTCTTGGGCTGTGAGCAGGGAACACCC CCGATCTTCTCTGTTGTGACTGCCCCCCTCTCTTGGGCTTGGGCTTGGGCTTGGGCTTGGGCT CTCATAAATCAACCCACGGCCCCAGGACACCGCACCACTGACCTGTGAGGTGAAGTTTCGCTGGA GCTGGTGTGACTACGGAGAGAACCATCCAGTCAACGTCACTATGTTCACAGAAACCAACAACT GGTATCTTTCCAGGAGATGGCTCAGGGAACCAAGAGACAGAGAGGAGTGGTTCATGSGGGCCATT GGAGGAGCTGGTGTACAGCCCTGCTCGCTCTTGTCTCTGCTCTCATCTTCTTATAGTGAAGACC CACAGGAGGAAAGCAGCCAGGACAGAGTGGGAGGAAATGACACCCACCTTACCACAGGCTCAGCC TCCCCGAAACACAGAAAGTCCAAGTTACATGGCCCCACTGAAACCTCAAGCTGTTACAGGTGCC GCCCCTACTGTGTGAGATGGATGAGGAGCTGCATTATGCTTCCCTCAACTTTTCATGGGATGAATCCT TCCAAGGACACCTTCCACCGAATACTCAGAGGTTCAGGACCCAGTCCGGGCTCATCACCATCATCAT TGA
146	CD33	human	aa	MGWSCIIILFLVATATGVHSDPNFWLQVQESVTVQEGLCVLVPCTFFHPIPYDKNSPVHGYWFREG AIIISGDSPVATNKLDOEVOEETQGRFRLLGLDPSRNNCSLSIDARRRDNNGSYFFRMRGSKYSYK

147	CD33	macaque	nt	SPQLSVHVTDLTHRPKILIPGTLEPGHSHKNIITCSVSWACEQGTPIIFSWLSAAPTSLGPRTHSSV LIITPRPDHGTNLTQVKFAGAGVTTERTIQLNVTVYVQNPPTGIFPGDSGKQETRAGVVHGAI GGAGVTALLALCLCLIFFIVKTHRRKAARTAVGRNDTHPTTGSASPKHQKSKLHGPTETSSCSGA APTVEDEELHYASLNFHGMNPSKDTSTEYSEVVRTQSGHHHHHH ATGCCGCTGCTGCTACTGCTGCCCTGCTGTGGGCAGGGCCCTGGCTATGGATCCAAAGATCAGG CTGGAAGTGCAGGAGTCACTGACAGTACAGGAGGGTTGTGCGTCTTGTGCCCTGCACTTTCTTC CATCCCGTACCCCTACCACACAGGAATCCCCAGTTTCCAGTTTACTGTTTACTGTTTCCGGGAAGGAGCCATT GTATCCTTGGAATCTCCAGTGGCCACAAACAAAGTAGATCAAGAAGTACAGGAGGAGACCCAGGGC CGATTCGCGCTCCTTGCGGATCCCAGTAGGAACAACTGCTCCCTTGAGCATCGTAGATGCCAGGAGG AGGATAAACGGTTTCATCTTCTCGGATGGAGAAAGAAAGTACCAATACAGTTACAAATCTTACC CAGCTCTGTGATGTGACAGACTTGACCCACAGGCCCAAACTCTCATCTCCCTGGAGCCCTAGAC CCTGACCACCTCCAAAAAACCCTGACCTGCTCTGTGCCCCCTGGGCTGTGAGCAGGGAACACCTCCAAATC TTCTCCTGGATGTACGTGCCCCACCTCCCTGGGCTCAGGACCACCTCACTCTCCCTCGGTGCTCATA ATCACCCACGGCCCCAGGACACGGCACCACTCACCTGTCAAGTGAAGTTCCCTGGAGCTGGC GTGACCACGGAGAGAACCATCCAGCTCAATGTCTCTTATGCTTACAGAACCCAAAGAACTGATATC TTTCTAGGAGACGGCTCAGGGAACAAAGAGTGGTTTACAGGAGCCATCGGGGAGCTGGTGTACACA GTCCGTGCTCTTTGCTCTGCTCATCTTCTTACAGTGAAGACTCACAGGAGGAAAGCAGCC AGGACAGCAGTGGGCAGGATCGACACCCACCCGCCACAGGGCCAACTCTCGAAACACACAGAAG AAGTCCAAAGTTACATGGGCGCACTGAAACCTCAGGCTGTTCAGGTACCACTTACTGTGGAGATG GATGAGAGCTGCATACGCTTCCCTCAACTTTTCATGGGATGAATCTTCTGAGGACACCTCCACC GAATACTCAGAGTCAAGACCCAGTGA
148	CD33 UD H2C HL x AF5 HL	artificial	aa	EVQLVESGGGLVQPGSLKLSCAAAGFTFNKYAMNWNVRQAPGKGLEWVARIRSKYNNYATYYADSV KDRFTISRDDSKNTAYLQMNLIKTEDTAYYCVRHGNFGNSYISYWAYWGQGLVTIVSSGGGSGG GGSGGGSTVVTQEPSTVSPGGTVTLTCSSTGAVTSYYPNWVQQKPGQAPRGLIGGTFKFLAP GTPARFSGSLLGKKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGLTLVLSGGGGSQVQLVQSGA EVKKPGASVKVSKASGYTFITNYGMNWVKQAPGQGLKWMGWINTYTGEPTYADDKGRVTMTSDTS TSTAYLELHNLRSDDTAVYYCARWSWSDGYVYFDYWGQGTITVTVSSg9g9gsg9g9gsDIVM TQSPDSLTVSLGERTTINCKSSQSVLDSKNKNSLAWYQQKPGQPPKLLLSWASTRESGIPDRFSG SGSGTDFTLTIDSLQPEDSATYCYCQQAHPFITFGQGRLEIK
149	CD33 UD H2C HL x AF5 HL	artificial	nt	GAGGTGCAGCTGGTCGAGTCTTGAGAGAGGATTTGGTGCAGCCTTGAGGGGTCAATTGAAACTCTCATGT GCAGCCTCTGGATTCACCTTCAATAAGTACGCCATGAATCGGGTCCGCCAGGCTCCAGGAAAAGGGT TTGGAATGGGTTGCTCGCATAAAGAGTAAATATAATTAATATGCAACATATATATGCCGATTCAGTG AAAGACAGGTTACCATCTCCAGAGATGATTCAAAAAACACATGCCCTATCTACAAATGAACAACTTG AAAACTGAGGACACTGCCGTGTACTGTGTGAGACATGGGAACCTTCGGTAATAGTACATATCC TACTGGGCTTACTGGGGCCAAAGGACTCTGGTACCCGCTCCTCAGGTGGTGGTGGTCTTGGCGGC GGCGGCTCCGGTGGTGGTTCTCAGACTGTGTGACTCAGGAACCTTCACCTACCGTATCACCT GGTGGAAACAGTCACACTCACTTGTGGCTCCTCGACTGGGGCTGTTACATCTGGCTACTACCCAAAC TGGGTCCAAACAAAAACCAGGTCAAGCACCCCGTGGTCTAATAGGTGGGACTAAGTTCTCTCGCCCCC

150	CD33 UD F12Q HL x AF5 HL	artificial	aa	GGTACTCCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCCCTCTCAGGGGTA CAGCCAGAGGATGAGGCAGAAATATTACTGTGCTCTATGGTACAGCAACCGTGGGTGTTTCGGTGA GGAACCAAACTGACTGTCTTATCCGGAGGTGGTGGCTCCAGGTGCAGTGGTCCAGTCTGGAGCT GAGGTGAAGAACCTGGAGCGTCAGTCAAGGTCTCTTGAAGGCTAGCGGTATACCTTTCACAAAC TATGGAATGAATGGTGAAGCAGGCTCCAGGACAGGTTTAAAGTGGATGGGTGGATAAACACC TACACTGGAGAGCAACATATGCTGATGACTTCAAGGACGGGTACCATGACTTCGGATACCTCT ACCAAGCACTGCTTATTTGGAATCCACAACCTCAGAACTGATGACACGGTGTATATATTGTGCG CGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTGTACTTGGGGCCAAGGCAC'TACGGTCAAC GTCTCCTCAGGTGGTGGTTCTTGGCGCGCGGCTCCGGTGGTGGTGGTCTTGACATCGTGATG ACACAGTCTCCAGACTCCCTGACTGTGCTCTTGGCGGAGAGGACCACTCAACTGCAAGTCCAGC CAGAGTGTTTTAGACAGCTCCAAGAAATAAGAACTCTTACTTTGGTACACAGCAAAACCCAGGACAG CCTCTAAATTTACTCTCTTCTGGGCATCTACCGGGGAA'TCCGGGATCCCTGACCGATTCACTGGC AGCGGGTCTGGGACAGATTTCACTCTCACTATTGACAGCTTCAGCCTGAAGATTCTGCAACTTAC TATTGTCAACAGTCTGCCCACTTCCCGATCACCTTTGGCCAAAGGACACGACTGGAGATTAAA EVQLVESGGGLVQPGGSLKLSCAAASGFTFNISYAMNWVRQAPKGLEWVARIRSKYNNIYATYYADSV KGRFTISRDDSKNTAYLQMNNLKLTEDTAVYYCVRHGNFGNSYVSWWAYWGQGLTVTVSSGGGSGG GGSGGGGQTVVTQEPSTLTVSPGGTVTLTLCGSSTGAVTSGNYPNWWQKPGQAPRGLIIGTKFLAP GTPARFSGSLLLGKAAALTLGSGVQPEDEAEFYCVLMYSNRWVFGGKTCLTVLSGGGGSQVQLVQSGA EVKKPGASVKVSCKASGYTFNRYGMNWVKQAPQGQGLKMWGINITYTGEPTYADDFKGRVTMTSDTS TSTAYLELHNLRSDDTAVYYCARWSWDGYVYFYDWQGTTVTVSSg999s9999s9999sD1VM TQSPDSLTVSLGERTTINCKSSQSVLDSKNKNSLAWYQKPGQPPKLLLSWASTRESGIPDRFSG SGSGTDFTLTIDSLQPEDSATYYCQQSAHFPITFGQGRLEIK
151	CD33 UD F12Q HL x AF5 HL	artificial	nt	GAGGTGCAGCTGGTCGAGTCTGGAGGAGGATTGGTGCAGCCTGGAGGGTCATTGAAAAC'TCTCATGT GCAGCCTCTGGATTCACTTCAATAGCTACGCCATGAAC'TGGGTCCGCCAGGCTCCAGGAAAAGGCT TTGGAATGGGTGGCTCGCATAGAAGTAATAATAATAATAATATGCAACATATATTATGCCGATTCACTG AAAAGCAGGTTTCAACATCTCCAGAGATGATTCAAAAAACACTGCC'TATCTACAAATGAACAACTTG AAAACTGAGGACACTGCCGTGTACTGTGTGAGACATGGGAACTTCGGTAATAGCTACGTTTCC TGGTGGGCTTACTGGGCGCAAGGACTCTGGTCAACCGTCTCCTCAGGTGGTGGTGTCTTGCGGC GGCGCTCCGGTGGTGGTGTCTCAGACTGTGTGTACTCAGGAACCTTCAC'TCACCGTATCACCT GGTGAACAGTCACACTCACTTGTGGCTCCTCGACTGGGGCTGT'TACATCTGGCAACTACCCAAAC TGGGTCCAAACAAAAACAGGTCAAGCACCCCGTGGTCTAAATAGGTGGGACTAAGT'TCCTCGCCCC GGTACTCTTCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGTCGCCCTCACCCCTCTCAGGGGTA CAGCCAGAGGATGAGGCAGAAATATTACTGTGTCTTATGGTACAGCAACCGTGGGTGTTTCGGTGA GGAACCAAACTGACTGTCTTATCCGGAGGTGGTGGCTCCCGAGGTGCAGTGGTCCAGTCTGGAGCT GAGGTGAAGAACCTGGGTGAAGCAGGCTCCAGGACAGGTTTAAAGTGGATGGGTGGATAAACACC TATGGAATGAATGGGTGAAGCAGGCTCCAGGACAGGTTTAAAGTGGATGGGTGGATAAACACC TACACTGGAGAGCAACATATGCTGATGACTTCAAGGACGGGTACCATGACTTCGGATACCTCTCT

152	CD33 UD I2C HL x AF5 HL	artificial	aa	ACCAGCACTGCCATTATTGGAACCTCCACAACTCAGAACTGATGACACGGCTGTATATTACTGTGCG CGCTGGAGTTGGAGTGTGTTACTACGTTTACTTTGACTACTTGGGGCCAAGGCACACTACGGTCACC GTCCTCCAGGTGGTGGTGGTTCGGCGCGCGGCTCCGGTGGTGGTGGTTCGTGACATCGTGATG ACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAGAGGACCACCATCAACTGCAAGTCCAGC CAGAGTGTTTTAGACAGCTCCAAGAATAAGAACTCCTTAGCTTGGTACCAGCAGAAACCCAGGACAG CCTCCTAAATTAATCTCCTTCCCTGGGCATCTACGCGGAATCCGGGATCCCTGACCGGATTCAGTGGC AGCGGCTCGGACAGATTTCACTCTCACTATTGACAGCTGCAGCTGAAGATTCGCAACTTAC TATTGTCAACAGTCTGCCCACTTCCCCGATCACCTTTGGCCAAAGGACACGACTGGAGATTAAA EVQLVESGGGLVQPGSLKLSCAAAGFTFNKYAMNWRQAPKGLWVARIIRSKYNNYATYYADSV KDRFTISRDDSKNTAYLQMNLIKTEDTAVYYCVRHGNFGNSYISYWAYWGQGLVTVSSGGGSGG GGSGGGGSGTVVTVQEPSTLVSPGGTVTLTCSSTGAVTSNYPNWVQKPGQAPRGLIGGTFKFLAP GTPARFSGSLGGKAAALTLISGVQPEDEAEYYCVLWYSNRWVFGGKTLTVLSGGGGSQVQLVQSGA EVKKPGASVKVSKASGYTFINYGMNWVKQAPGQGLKWMGWINTYTGEPTYADDFKGRVTMTSDTS TSTAYLELHNLRSDDTAVYYCARWSWSDGYVYFDYWGQGTITVTVSSg999s9999sDIVM TQSPDSLTVSLGERTTINCKSSQSVLDSKKNKNSLAWYQQKPGQPPKLLLSWAISTRESGIPDRFSG SGSGTDFTLTIDSLQPEDSATYFCQQSAHFPITFGQGTGLEIK
153	CD33 UD I2C HL x AF5 HL	artificial	nt	GAGGTGCAGCTGGTCGAGTCTGGAGGAGGATTTGGTCAGCCTTGAGGGTCATTGAAACTCTCATGT GCAGCCTCTGGGATTCACCTTCAATAAGTACGCCATGAACCTGGGTCCGCCAGGCCTCCAGGAAAAGGT TTGGAATGGGTGGTCGCATAAAGAAGTAAATATAATAATATGCAACATATATGCGGATTCAGTG AAAGACAGGTTCAACATCTCCAGAGATGATTCAAAAAACAACCTGCCATCTACAAAATGAACAACCTTG AAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGGAACTTCGGTAATAGCTACATATCC TACTGGGCTTACTGGGGCCAAAGGACTCTGGTCACCGTCTCCTCAGGTGGTGGTGTCTGGCGGC GGCGGCTCCGGTGGTGGTTCACAGACTGTGTGACTCAGGAACTTCACCTACCGTATCACCT GGTGGAAACAGTCACACTCACTTGTGGCTCCTCGACTGGGGCTGTTACATCTGGCAACTACCCAAAC TGGGTCCAAACAAAAACAGGTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTCTCGCCCCC GGTACTCCTGCCAGATTCTCAGGCTCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTA CAGCCAGAGGATGAGGCAGAAATATTACTGTGTCTTATGGTACAGCAACCGCTGGGTGTTTCGGTGA GGAAACCAAACTGACTGTCTTATCCGGAGGTGGTGGTCCCAGGTGCAGCTGGTCCAGTCTGGAGCT GAGGTGAAGAAGCCTGGAGCGTCAGTCAAGGTCTCCTGCAAGGCTAGCGGGTATACCTTCACAAAC TATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGGTTTAAAGTGGATGGGTGGATAAACACC TACACTGGAGAGCCAAACATATGCTGATGACTTCAAGGACGGGTACCATGACTTCGGATACCTCT ACCAGCACTGCCATTATTGGAACCTCCACAACCTCAGAACTGACACGGTGTATATATTACTGTGCG CGCTGGAGTTGGAGTGTGTTACTACGTTTACTTTGACTACTTGGGGCCAAAGGCATACGGTCACC GTCCTCCAGGTGGTGGTTCGGCGCGCGGCTCCGGTGGTGGTGGTTCGTGACATCGTGATG ACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAGAGGACCACCATCAACTGCAAGTCCAGC CAGAGTGTTTTAGACAGCTCCAAGAATAAGAACTCCTTAGCTTGGTACCAGCAGAAACCCAGGACAG CCTCCTAAATTAATCTCCTTTCCTGGGCATCTACGCGGGAATCCGGGATCCCTGACCGGATTCAGTGGC

				AGCGGGTCTGGGACAGATTTCACCTCTACATATTGACAGCCTGCAGCCTGAAGATTCTGCAACTTAC TATTGTCAACAGTCTGCCACTTCCCGATCACCTTTGGCCAAAGGACACGACTGGAGATTAAA
154	VL of F6A	artificial	aa	QTVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTL SGVQPEDEAEYICALWYSNRWVFGGGTKLTVL
155	VH of F6A	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KSRFTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGNFGNSYVSFFAYWGQGTLLTVSS
156	VH-VL of F6A	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KSRFTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGNFGNSYVSFFAYWGQGTLLTVSSGGGSGG GGSGGSGQTVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAALTL SGVQPEDEAEYICALWYSNRWVFGGGTKLTVL
157	VL-P of F6A	artificial	aa	ELVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTL SGVQPEDEAEYICALWYSNRWVFGGGTKLTVL
158	VH-P of F6A	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KSRFTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGNFGNSYVSFFAYWGQGTLLTVSS
159	VH-VL-P of F6A	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KSRFTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGNFGNSYVSFFAYWGQGTLLTVSSGGGSGG GGSGGSELVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAALTL SGVQPEDEAEYICALWYSNRWVFGGGTKLTVL
160	VL of H2C	artificial	aa	QTVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTL SGVQPEDEAEYICALWYSNRWVFGGGTKLTVL
161	VH of H2C	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KDRFTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGNFGNSYISYWAYWGQGTLLTVSS
162	VH-VL of H2C	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KDRFTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGNFGNSYISYWAYWGQGTLLTVSSGGGSGG GGSGGSGQTVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAALTL SGVQPEDEAEYICALWYSNRWVFGGGTKLTVL
163	VL-P of H2C	artificial	aa	ELVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTL SGVQPEDEAEYICALWYSNRWVFGGGTKLTVL
164	VH-P of H2C	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KDRFTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGNFGNSYISYWAYWGQGTLLTVSS
165	VH-VL-P of H2C	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KDRFTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGNFGNSYISYWAYWGQGTLLTVSSGGGSGG GGSGGSELVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAALTL SGVQPEDEAEYICALWYSNRWVFGGGTKLTVL
166	VL of H1E	artificial	aa	QTVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTL SGVQPEDEAEYICALWYSNRWVFGGGTKLTVL
167	VH of H1E	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KDRFTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGNFGNSYISYWAYWGQGTLLTVSS

168	VH-VL of H1E	artificial	aa	EVQLVESGGGLEQPGGSLKLSCAASGFTFNISYAMNWVRQAPGKGLEWVARIRSKYNNIYATYYADSV KGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTILVTVSSGGGSGG GGSGGGGQTVVTQEPSTVSPGGTVTLTCGSSTGAVTSGYYPNWVQOKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAALTLVGQVQPEDEAEYFCALWYSNRWVFGGTTKLTIVL
169	VL-P of H1E	artificial	aa	ELVVTQEPSTVSPGGTVTLTCGSSTGAVTSGYYPNWVQOKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTLVGQVQPEDEAEYFCALWYSNRWVFGGTTKLTIVL
170	VH-P of H1E	artificial	aa	EVQLLESVGGGLEQPGGSLKLSCAASGFTFNISYAMNWVRQAPGKGLEWVARIRSKYNNIYATYYADSV KGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTILVTVSS
171	VH-VL-P of H1E	artificial	aa	EVQLLESVGGGLEQPGGSLKLSCAASGFTFNISYAMNWVRQAPGKGLEWVARIRSKYNNIYATYYADSV KGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTILVTVSSGGGSGG GGSGGGSELVVTQEPSTVSPGGTVTLTCGSSTGAVTSGYYPNWVQOKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAALTLVGQVQPEDEAEYFCALWYSNRWVFGGTTKLTIVL
172	VL of G4H	artificial	aa	QTVVTQEPSTVSPGGTVTLTCGSSTGAVTSGYYPNWVQOKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTLVGQVQPEDEAEYFCALWYSNRWVFGGTTKLTIVL
173	VH of G4H	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAASGFTFNRYAMNWVRQAPGKGLEWVARIRSKYNNIYATYYADSV KGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTILVTVSS
174	VH-VL of G4H	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAASGFTFNRYAMNWVRQAPGKGLEWVARIRSKYNNIYATYYADSV KGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTILVTVSSGGGSGG GGSGGGGQTVVTQEPSTVSPGGTVTLTCGSSTGAVTSGYYPNWVQOKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAALTLVGQVQPEDEAEYFCALWYSNRWVFGGTTKLTIVL
175	VL-P of G4H	artificial	aa	ELVVTQEPSTVSPGGTVTLTCGSSTGAVTSGYYPNWVQOKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAALTLVGQVQPEDEAEYFCALWYSNRWVFGGTTKLTIVL
176	VH-P of G4H	artificial	aa	EVQLLESVGGGLVQPGGSLKLSCAASGFTFNRYAMNWVRQAPGKGLEWVARIRSKYNNIYATYYADSV KGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTILVTVSS
177	VH-VL-P of G4H	artificial	aa	EVQLLESVGGGLVQPGGSLKLSCAASGFTFNRYAMNWVRQAPGKGLEWVARIRSKYNNIYATYYADSV KGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTILVTVSSGGGSGG GGSGGGSELVVTQEPSTVSPGGTVTLTCGSSTGAVTSGYYPNWVQOKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAALTLVGQVQPEDEAEYFCALWYSNRWVFGGTTKLTIVL
178	VL of A2J	artificial	aa	QTVVTQEPSTVSPGGTVTLTCRSSTGAVTSGYYPNWVQOKPGQAPRGLIGATDMRPSGTPARFSG SLLGGKAALTLVGQVQPEDEAEYFCALWYSNRWVFGGTTKLTIVL
179	VH of A2J	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAASGFTFNRYAMNWVRQAPGKGLEWVARIRSKYNNIYATYYADSV KGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTILVTVSS
180	VH-VL of A2J	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAASGFTFNRYAMNWVRQAPGKGLEWVARIRSKYNNIYATYYADSV KGRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYLSFWAYWGQGTILVTVSSGGGSGG GGSGGGGQTVVTQEPSTVSPGGTVTLTCRSSTGAVTSGYYPNWVQOKPGQAPRGLIGATDMRPS GTPARFSGSLLGGKAALTLVGQVQPEDEAEYFCALWYSNRWVFGGTTKLTIVL
181	VL-P of A2J	artificial	aa	ELVVTQEPSTVSPGGTVTLTCRSSTGAVTSGYYPNWVQOKPGQAPRGLIGATDMRPSGTPARFSG SLLGGKAALTLVGQVQPEDEAEYFCALWYSNRWVFGGTTKLTIVL

182	VH-P of A2J	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAAASGFTFNKYAMNVRQAPGKGLWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYLSWYAYWGQGTLLVTVSS
183	VH-VL-P of A2J	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAAASGFTFNKYAMNVRQAPGKGLWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYLSWYAYWGQGTLLVTVSSGGGGSGG GGGGGGSELVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPS GTPARFSGLLGGKAALTLVGQPEDEAEYCALWYSNRWVFGGTTKLTIVL
184	VL of E1L	artificial	aa	QTVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPSGTPARFSG SLLGGKAALTLVGQPEDEAEYCALWYSNRWVFGGTTKLTIVL
185	VH of E1L	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAAASGFTFNKYAMNVRQAPGKGLWVARIRSKYNNYATYYADSV KSRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYTSYAYWGQGTLLVTVSS
186	VH-VL of E1L	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAAASGFTFNKYAMNVRQAPGKGLWVARIRSKYNNYATYYADSV KSRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYTSYAYWGQGTLLVTVSSGGGGSGG GGGGGGQTVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPS GTPARFSGLLGGKAALTLVGQPEDEAEYCALWYSNRWVFGGTTKLTIVL
187	VL-P of E1L	artificial	aa	ELVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPSGTPARFSG SLLGGKAALTLVGQPEDEAEYCALWYSNRWVFGGTTKLTIVL
188	VH-P of E1L	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAAASGFTFNKYAMNVRQAPGKGLWVARIRSKYNNYATYYADSV KSRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYTSYAYWGQGTLLVTVSS
189	VH-VL-P of E1L	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAAASGFTFNKYAMNVRQAPGKGLWVARIRSKYNNYATYYADSV KSRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYTSYAYWGQGTLLVTVSSGGGGSGG GGGGGGSELVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPS GTPARFSGLLGGKAALTLVGQPEDEAEYCALWYSNRWVFGGTTKLTIVL
190	VL of E2M	artificial	aa	QTVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPSGTPARFSG SLLGGKAALTLVGQPEDEAEYCALWYSNRWVFGGTTKLTIVL
191	VH of E2M	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAAASGFTFNKYAMNVRQAPGKGLWVARIRSKYNNYATYYADSV KERFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYLSWYAYWGQGTLLVTVSS
192	VH-VL of E2M	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAAASGFTFNKYAMNVRQAPGKGLWVARIRSKYNNYATYYADSV KERFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYLSWYAYWGQGTLLVTVSSGGGGSGG GGGGGGQTVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPS GTPARFSGLLGGKAALTLVGQPEDEAEYCALWYSNRWVFGGTTKLTIVL
193	VL-P of E2M	artificial	aa	ELVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPSGTPARFSG SLLGGKAALTLVGQPEDEAEYCALWYSNRWVFGGTTKLTIVL
194	VH-P of E2M	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAAASGFTFNKYAMNVRQAPGKGLWVARIRSKYNNYATYYADSV KERFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYLSWYAYWGQGTLLVTVSS
195	VH-VL-P of E2M	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAAASGFTFNKYAMNVRQAPGKGLWVARIRSKYNNYATYYADSV KERFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYLSWYAYWGQGTLLVTVSSGGGGSGG GGGGGGSELVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPS GTPARFSGLLGGKAALTLVGQPEDEAEYCALWYSNRWVFGGTTKLTIVL

196	VL of F70	artificial	aa	QTVVTQEPSTLVSPGGTTLTTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
197	VH of F70	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYISWWAYWGQGTLLTVSS
198	VH-VL of F70	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYISWWAYWGQGTLLTVSSGGGSGG GGSGGGSGTAVVTQEPSTLVSPGGTTLTTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
199	VL-P of F70	artificial	aa	ELVVTQEPSTLVSPGGTTLTTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
200	VH-P of F70	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYISWWAYWGQGTLLTVSS
201	VH-VL-P of F70	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYISWWAYWGQGTLLTVSSGGGSGG GGSGGGSELVVTQEPSTLVSPGGTTLTTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
202	VL of F12Q	artificial	aa	QTVVTQEPSTLVSPGGTTLTTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
203	VH of F12Q	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYISWWAYWGQGTLLTVSS
204	VH-VL of F12Q	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYISWWAYWGQGTLLTVSSGGGSGG GGSGGGSGTAVVTQEPSTLVSPGGTTLTTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
205	VL-P of F12Q	artificial	aa	ELVVTQEPSTLVSPGGTTLTTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
206	VH-P of F12Q	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYISWWAYWGQGTLLTVSS
207	VH-VL-P of F12Q	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYISWWAYWGQGTLLTVSSGGGSGG GGSGGGSELVVTQEPSTLVSPGGTTLTTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAP GTPARFSGSLLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
208	VL of I2C	artificial	aa	QTVVTQEPSTLVSPGGTTLTTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL
209	VH of I2C	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYISWWAYWGQGTLLTVSS
210	VH-VL of I2C	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSV KKRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYISWWAYWGQGTLLTVSSGGGSGG GGSGGGSGTAVVTQEPSTLVSPGGTTLTTCGSSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAP

211	VL-P of I2C	artificial	aa	GTPARFSGSLGKKAALTLSGVQPEDEAEYYCVLMYSNRWVFGGGTKLTVL ELVVTFQEPSTVSPGGTVTLTCGSSGTGAVTSGNYPNWVQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGKKAALTLSGVQPEDEAEYYCVLMYSNRWVFGGGTKLTVL
212	VH-P of I2C	artificial	aa	EVQLLFSGGGLVQPGSLKLSCAAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSV KDRFTISRDDSKNTAYLQMNILKTEDTAVYVCVRHGNFGNSYISYWAYWGQGTIVTVSS
213	VH-VL-P of I2C	artificial	aa	EVQLLFSGGGLVQPGSLKLSCAAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSV KDRFTISRDDSKNTAYLQMNILKTEDTAVYVCVRHGNFGNSYISYWAYWGQGTIVTVSSGGGSGG GGSGGGSELVVTQEPSTVSPGGTVTLTCGSSGTGAVTSGNYPNWVQKPGQAPRGLIGGTKFLAP GTPARFSGSLGKKAALTLSGVQPEDEAEYYCVLMYSNRWVFGGGTKLTVL
214	SA21-CD33 E11 HL x I2C HL (His Tag)		nt	CGCCTGATTGAAGATATTTGCCCTGCCGCGCTGGGCTGCCCTGTGGGAAGATGAT CAGGTGCAGCTGGTGAGTCTGGAGCTGAGGTGAAGAAAGCCTGGAGAGTCAGTCAAGGTCTCCTGTC AAGGCTAGCGGGTATACCTTCACAAAACATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACCTACACTGGAGAGCAACCTATGCTGATAAAGTTCCAGGGA CGGTTACCATGACTACGGATACCTCTACACAGCACTGCCCTATATGGAATAACCGCAACCTCGGAGGT GATGACACGGCTGTATATTTACTGTGCGCGCTGGAGTTGGAGTGGTTACTACGTTTACTTTTGAC TACTGGGGCCAAAGCACTTCGGTCACCGCTCCTCAGGTGGTGGTTCTGGCGGGCGGGCTCC GGTGGTGGTGGTTCTGACATCGTATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCAACATCAACTGCAAGTCCAGCCAGAGTGTATTTAGACAGCTCCACGAATAAGAACTCCTTA GCTTGGTACCAGAGAAAACAGGACAGCTCCTAAATTAATCTCTTCTGGGCATCTACGCGGGA TCCGGGATCCCTGACCGATTTCAGTGGCAGCGGTCTGGGACAGATTTCACTCTCACTATTGACAGC CCGAGCCTGAAAGATTCTGCAACTTACTATTTGTAACAGTCTGCCACTTCCCGATCACTTTGGC CAAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGTCCGAGGTGCAGTGGTCGAGTCTGGA GGAGGATTGGTGAGCTGGAGGGTCAATTGAAACTCTCATGTGCAGCTCTTGATTCACCTTCAAT AAGTACCCCATGAACCTGGGTCCCGCAGGCTCCAGGAAAGGGTTTGGAAATGGGTGCTCGCATAAAGA AGTAAATATAATTAATGCAACATATTTATGCCGATTTCAGTGAAAGACAGGTTACCATCTCCAGA GATGATTCAAAAAACACTGCCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACCTTCGGTAAATAGCTACATATCTTACTGGGCTTACTGGGGCCAAAGG ACTCTGGTCAACCGTCTCCTCAGGTGGTGGTGTCTTGGCGCGCGCGCTCCGGTGGTGGTGGTCTT CAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACTTGGTGAACAGTCACACTCACTTGT GGCTCCTCGACTGGGCTGTACATCTGGCAACTACCAAACTGGGTCCCAACAAACCAAGGTCAG GCACCCCGTGGTCTAATAGGTGGACTAAGTTCCCTGCCCGGCTACTCTGCCAGATTCTCAGGC TCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGTCTATGGTACAGCAACCGCTGGGTGTTCGGTGGAGGAACCAAACTGACTGTCTCTA CATCACCATCACCATCAC
215	SA21-CD33 E11 HL x I2C HL H6		aa	RLIEDICLPRWGLWEDDQVQLVQSGAEVKKPESVKVSCKASGYFTNYGMNWVKQAPGQGLEWM GWINTYTGEPTYADKFQGRVTMTTDTSTAYMEIRNLGGDDTAVYCARWSWSDGYVYFYDWGQ GTSVTVSSGGGGGGGGSDIVMTQSPDSLTVSLGERTTINCKSSVLDSSSTNKNLSLAWYQ QKPGQPPKLLLSWASTRESGIPDRFSGSGSGTDFTLTIDSPQEDSATYYCQSAHFPITFTGQGT LEIKSGGGGSEVQLVESGGGLVQPGSLKLSCAAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYN

				NYATYYADSVKDRFTTISRDDSKNTAYLQMNLLKTEDTAVYCYVRHGNFNSYISYWAYWGQGLVTVTSVSSGGSGGGSGGGSGQTVVTQEPSTVSPGGTVTLTTCGSSTGAVTSGNYPNWVQOKPGQAPRG LIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQVPEDEAEYYCVLWYSNRWVFGGGTKLTVLHHHHH H
216	SA25-CD33 E11 HL x 12C HL with His tag		nt	GAGGACATCTGCCTGCCAGATGGGGCTGCCCTGTGGGAGGACCAGGTGCAGCTGGTGCAGTCTGGA GCTGAGGTGAAGAAGCCTGGAGAGTCAGTCAAGGTCTCCTGCAAGGTAGTCGGGTATACCTTCACA AACTATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGGTTTAGAGTGGATGGGTGGATAAAC ACCTACACTGGAGAGCCAACTATGCTGATAAGTTCAGGGACGCTTACCATGATACGGATACC TCTACCAGCACTGCCATATATGGAATCCGCAACTCGGAGGTGATGACACGGCTGTATATTACTGT GCGCGTGGAGTTGGAGTGTGTTTCTGGCGCGCGGCTCCGGTGGTGGTGGTGGTGGTGGTGGTGGT ACCGTCTCCTCAGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT ATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAGAGGACCACTCAACTGCAAGTCC AGCCAGAGTGTTTTAGACAGTCCACGAATAAGAACTCCTTAGCTTGGTACCAAGCAAAACCAAGGA CAGCCTCCTAAATTACTCCTTCTGGGCATCTACGCGGGAATCCGGGATCCCTGACCGATTCACT GGCAGCGGGTCTGGGACAGATTTCACTCTCACTATTGACAGCCCGCAGCCTGAAGATTCTGCAACT TACTATTGTCAACAGTCTGCCCACTTCCCGATCACCTTTGGCCAAAGGACACGACTGGAGATTAAAA TCCGGAGGTGGTGGCTCCGAGGTGCAGCTGGTCGAGTCTTGAGGAGGATGGTGCAGCCTGGAGGG TCATTGAAAACCTCTCATGTGCAGCCTCTGGATTACCTTCAATAAGTACGCATGAACTGGGTCCGC CAGGCTCCAGGAAAAGGGTTTGGAAATGGGTTCGTCGCATAAGAAATGTAATAATAATAATAATA TATTATGCCGATTTCAGTGAAGACACAGGTTCACTCTCCAGAGATGATTCAAAAAACCACTGCCCTAT CTACAAATGAACAACCTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGGAACTTC GGTAATAGTACATACTCTACTGGGCTTACTTGGGGCCAAAGGACTCTGGTCACTCTCTCTCTCTCT GGTGGTGGTCTTGGCGGGCGGCTCCGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT TCACTCACCGTATCACCTGGTGGAAACAGTACACATCACTTGTGGCTCTCTCGACTGGGGCTGTACA TCTGGCAACTACCCAACTGGGTCCAAACAAAAACAGGTACAGGACCCCCGTGGTCTAAATAGTGGG ACTAAGTTCTCGCCCCCGTACTCTCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGCTGCC CTCACCTCTCAGGGGTACAGCCAGAGGATGAGGAGAAATATTACTGTGTCTATGTTACAGCAAC CGCTGGGTGTTCTGGTGGAGGAACCAAACTGACTGTCTCTA CATCACCATCACCATCAC
217	SA25-CD33 E11 HL x 12C HL H6		aa	EDICLPRWGCLWEDQVLVQSGAEVKKPGEVSKVSKASGYTFTNYGMWVWVQAPGQGLWGMWIN TYTGEPTYADKFQGRVTMTTDTSTSTAYMEIRNLGGDDTAVYCARWSWSDGYVYVYDFYWGQGTSV TVSSGGSGGGSGGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSTNNKNSLAWYQOKPG QPPKLLLSWASTRESGIPDRFSGSGSGTDFTLTIDSPQPEDSATYCYQSAHFPITTFGQGTRELEIK SSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMWVVRQAPGKLEWVARIRSKYNNYAT YYADSVKDRFTISRDDSKNTAYLQMNLLKTEDTAVYCYVRHGNFNSYISYWAYWGQGLVTVTSVSSG GGSGGGSGGGSGQTVVTQEPSTVSPGGTVTLTTCGSSTGAVTSGNYPNWVQOKPGQAPRGLIGG TKFLAPGTPARFSGSLLGGKAALTLSGVQVPEDEAEYYCVLWYSNRWVFGGGTKLTVLHHHHHH
218	SA08-CD33 E11 HL x 12C HL with His tag		nt	CAGGGCTGATCGGCGACATCTGCCCTGCCAGATGGGGTGCCTGTGGGGCGACTCCCGTGAACAACAG GTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAACCTGGAGAGTCAGTCAAGGTCTCCTGCAAG GCTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAAGCGGGCTCCAGGACAGGGTTTA

				GAGTGGATGGGCTGGATAAAACACCTTACACTGGAGAGCCAAACCTATGCTGATAAGTTCCAGGGACGC GTTACCATGACTACGGATACCTCTACCAGCACTGCCATATATGGAATCCGCAACCTCGGAGGTGAT GACACGGCTGTATATTAATGTCGCGCTGGAGTTGGAGTGATGTTACTACGTTTACTTTGACTAC TGGGGCCAAAGGCATTCGGTCACCGTCTCCTCAGGTGGTGGTTCCTGGCGCGCGGCTCCGGT GGTGGTGGTTCGTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAGAGG ACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCACGAATAAGAACTCCTTAGCT TGGTACCAGCAGAAAAACAGGACAGCTCCTAAATTAATCTCTTCTGGGCATCTACGCGGAATCC GGATCCCTGACCGATTCAGTGGCAGCGGTCTGGACAGATTTCACTCTCACTATTTGACAGCCCG CAGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCAGTACACTTTGGCCAA GGACACGACTGGAGATTAAATCCGGAGGTGGTGGTCCGAGGTGACGTGGTCTGAGTCTGGAGGA GGATTGGTGCAGCTGGAGGTCAATTGAAACTCTCATGTGACAGCTCTGGATTCACTTCAATAAG TACGCCATGAACTGGGTCGCCAGGCTCCAGGAAAGGTTTGGAAATGGGTGCTCGCATAAAGAGT AAATATAATAATTATGCAACATATTATGCCGATTCAAGTGAAGACAGGTTACCATCTCCAGAGAT GATCAAAAAACACTGCCATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTACTAC TGTGTGAGACATGGGAACTTCGGTAATAGTACATATCTTACTGGCTTACTGGGCGCAAGGACT CTGGTCACCGTCTCCTCAGGTGGTGGTTCCTACCTACCGTATCACTGGTGGAAACAGTCACACTCACTGTGGC ACTGTTGTGACTCAGGAACTTCACTACCGTATCACTGGTGGCGCGGCTCCGGTGGTGGTCTCAG TCCTCGACTGGGCTGTACATCTGGCAACTACCCAACTGGGTCCAAACAAAAACAGGTCAGGCA CCCCGTGGTCTAATAGGTGGACTAAGTTCCCTCGCCCCCGGTACTCTCTGCCAGATTCTCAGGCTCC CTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATATTAC TGTGTTCTATGTTACAGCAACCGCTGGGTGTTCTGGTGGAGGAAACCAAACTGACTGTCTCTA CATCACCATCACCATCAC
219	SA08-CD33 E11 HL x I2C HL H6		aa	QGLIGDILPRWGLWDSVKQVLVQSGAEVKKPGEVSKVSKASGYFTFNYGMNVWKQAPQGL EWMGWINTYTGEPTYADKFQGRVTMTTDTSTSTAYMEIRNLGGDDTAVYICARWSWSDGYVYFDY WGQGTSVTVSSGGGGSGGGGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSTNKNLSLA WYQQKPGQPPKLLLSWASTRESGIIPDRFSGSGSDTFTLTIDSPQPEDSATYCYCQSAHFPITFGQ GTRLEIKSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRS KYNMYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVVRHGNFGNSYISYWAYWGQGT LVTVSSGGGGSGGGSGGQTVVTQEPSTLTVSPGGTFTLTTCGSSTGAVTSGNYPNWVQKPGQA PRGLIGGPKFLAPGTPARFSGSLLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTLVHH HHHH
220	SA21-CD33 E11 HL x I2C HL		nt	CGCTGATTGAAGATATTTGCCCTGCCCGCTGGGGCTGCCCTGTGGGAAGATGATCAGGTGCAGCTG GTGCAGTCTGGAGCTGAGGTGAAGAACCTTGAGAGTCACTCAAGGTCTCTCTGCAAGGCTAGCGGG TATACCTTCACAAAATATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGTTTAGAGTGGATG GGCTGGATAAAACACCTACACTGGAGAGCCAACTATGCTGATGAATTCAGGGACGCGTTACCATG ACTACGGATACCTCTACCAGCACTGCCATATATGGAATCCGCAACCTCGAGGTGATGACACGGCT GTATATTACTGTGCGCGCTGGAGTTGGAGTGATGTTACTACGTTTACTTTGACTACTTGGGGCCAA GGCACTTCGGTCACCGTCTCCTCAGGTGGTGGTTCCTGGCGCGCGGCTCCGGTGGTGGTGGT TCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAGAGGACCAACCATC

				AACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCACGAAATAAGAACTCCTTAGCTTGGTACCAG CAGAAACAGGACAGCCTCCTAAATTAATCTCTCTTCTGGGCATCTACGGGGAATCCGGGATCCCT GACCGATTCAAGTGGCAGCGGCTTGGGACAGATTCTACTCTCACTATTGACAGCCCGCAGCCTGAA GATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGATCACTTTTGGCCAAGGACACGA CTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGTGGTCTGAGTCTGGAGGAGGATTGGTG CAGCCTGGAGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAATAAGTACGCCATG AACTGGGTCCGCGCAGGCTCCAGGAAAGGTTTGGAAATGGTGTCTGCATAAAGTAATAATAAT AATTATGCAACATATATGCCGATTCAAGTGAAGACAGGTTTCAACATCTCCAGAGATGATTCAAAA AACACTGCCATTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGA CATGGAACTTTCGGTAAATAGCTACATATCTACTTGGGCTTACTTGGGCAAGGACTCTTGGTCAAC GTCCTCAGGTGGTGGTGTCTTGGCGGCGGCTCCGGTGGTGGTGTCTTCAGACTGTGTGTG ACTCAGGAACCTTCACTCACCGTATCACTGGTGGAAACAGTCACTCACTTGTGGCTCCTCGACT GGGCTGTTACATCTGGCAACTACCCAACTGGGTCCAAACAAACAGGTCAAGCACCCCGTGGT CTAATAGGTGGGACTAAGTCTCTCGCCCCGGTACTCTCTGCCAGATTCTCAGGCTCCCTGCTTGA GGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGATATTAATGTGTCTTA TGGTACAGCAACCGCTGGGTGTTCGGTGGAGGAAACCAAACTGACTGTCTTA
221	SA21-CD33 E11 HL x I2C HL		aa	RLIEDICLPWGLWEDDQVLVQSGAEVKKPGESVKVSKCASGYTFTNYGMNWVKQAPGQGLEWM GWINYTGEPTYADKFQGRVTMTDTSTSTAYMEIRNLGGDDTAVYCARWSWSDGYVYFYFDYWGQ GTSVTVSSGGGGGGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSSTNKNLSLAWYQ QKPGPPKLLLSWASTRESGIPDRFSGSGSGTDFTLTIDSPQEDSATYQCQSAHFPIITFGQGT LEIKSGGGSEVQLVVESSGGLVQPGSLKLSAAAGTFTNRYAMNWRQAPKGLWVARIRSKYN NYATYYADSVKDRFTISRDDSKNTAYLQMNILKTEDTAVYYCVRHGNFGNSYISYWAYWGQGT VSSGGSGGGGGSGQTVVTQEPSTVSPGGTTLTTCGSSGTAVTSGNYPNWVQQKPGQAPRG LIIGGTFKFLAPGTPARFSGSLIGKKAALTLISGVQPEDEAEYYCVLMYSNRWVFGGGTKLTVL
222	SA25-CD33 E11 HL x I2C HL		nt	GAGGACATCTGCCGTGCCAGATGGGGCTGCCGTGGGAGGACCAAGGTGCAGCTGGTGCAGTCTGGA GCTGAGGTGAAGAACCTGGAGAGTCAGTCAAGGTCTCTCTGCAAGGCTAGCGGGTATACCTTCACA AACTATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGGTTTAGAGTGGATGGCTGGATAAAC ACCTACACTGGAGAGCAACCTATGCTGATAAGTTCAGGACGCGTTACCATGACTACGGATACC TCTACCAGCACTGCCATATATGAAATCCGCAACCTCGAGGTGATGACACGGCTGTATATTACTGT GCGGCTGGAGTTGAGTGATGTTACTACGTTTACTTGTACTTGGGGCCAAAGGCACTTCGGTC ACCGTCTCCTCAGGTGGTGGTGTCTTGGCGGCGCGGCTCCGGTGGTGGTGTCTTGACATCGTG ATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTTGGCGAGAGGACCACTCAACTGCAAGTCC AGCCAGAGTGTTTTAGACAGCTCCACGAAATAAGAACTCTTACTTGGTACGACGAGAAACCCAGGA CAGCTCCTAAATTAATCTCTTCTGGGATCTACGCGGAAATCCGGGATCCCTGACCCGATTCACT GGCAGCGGCTTGGGACAGATTTCACTCTCACTATTGACAGCCCGCAGCCTGAAAGATTCTGCAACT TACTATTGTCAACAGCTTGCCCACTTCCCGATCACTTTGGCCAAAGGACACGACTGGAGATTAAA TCCGAGGTGGTGGCTCCGAGGTGCAGCTGGTCTGAGTCTGAGGAGGATTGGTGCAGCCTGGAGGG TCATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAATAAGTACGCCATGAACCTGGGTCCGC CAGGCTCCAGGAAAGGTTTGGAAATGGTGTCTCGCATAAAGTAATAATAATAATATATGCAACA

223	SA25-CD33 E11 HL x I2C HL	aa	TATTATGCCGATTTCAGTGAAAACACAGGTTTACCATTCTCCAGAGATGATTCAAAAAACACTGCCTATCTACAAAATGAACAACCTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGGAACCTTGGTAATAGCTACATATCCTACTTGGGCTTACTTGGGGCCAAGGACTCTGGTCAACCTTCTCCTCAGGTGGTGGTGGTCTTGGCGCGCGGCTCCGGTGGTGGTGGTCTTCCAGACTGTTGTGACTCAGGAACCTTCACTACCCGTATACCTGGTGGAAACAGTCACTCACTTGTGGCTCCTCGACTGGGCTGTTTACA TCTGGCAACTACCCAAACTGGGTCCAAACAAAAACAGGTCAAGCACCCCGTGGTCTAATAGGTGGGACTAAAGTTCCCTCGCCCCGCTTCTTCCAGAGATTCAGGCTCCCTGCTTGAGGCAAGGCTGCCCTACCCCTCTCAGGGGTACAGCCAGAGGATGAGGACAGAATATTAATGTGTCTTATGGTACAGCAACCGCTGGGTGTCGGTGAGGAACCAAACTGACTGTCTCTA EDICLRMGCLWEDQVLVQSGAEVKKPGEISVKVSKASGYTFTNYGMNWNWKQAPGQGLEWMGWINTYTGEPTYADKFQGRVMTTDTSTSTAYMEIRNLGGDDTAVYYCARWSWSDGYVYFYFDYWGQGTSTVTVSSGGGSGGGSGGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSTNKNLSLAWYQQKPGQPPKLLLSWASTRESGIPDRFSGSGSGTDFTLTIDSPQPEDSATYYCQOQSAHFPITTFGQGTRELEIKSGGGSEVQLVVESGGLVQPGSLKLSCAAASGFTFNKYAMNWNVQAPGKGLEWVARIRSKYNNIYATYYADSVKDRFTTISRDDSKNTAYLQMNILKTEDTAVYYCVPRHGNFGNSYISYWAYWVGQGTILVTVSSGGGGSGGGSGGSGTQVVTQEPSTLTVSPGGTIVTITCGSSSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLAPGTPARFSGSLILGGKAAALTLGSGVQPEDEAEFYCVLMYSNRWVFGGKTLTVL CAGGGCTGATCGCGCACATCTGCCTGCCCAGATGGGGCTGCCTGTGGGGCGACTCCCGTGAAACAGGTGTCAGCTGGTGACGCTGGAGCTGAGGTGAAGAGCCTGGAGAGTCAGTCAAGGTCTCCTGCAAGGCTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAAGCAGGCTCCAGGACAGGGTTTAGAGTGGGTGGATGATAAAACACCTACACTGGAGAGCCAACTATGCTGATAAGTTCCAGGGACGCGTTACCATGACTACGGATACCTCTACCAGCACTGCCCTATATGGAATAACCGCAACCTCGGAGGTGATGACCGCTGTATATTAATGTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGACTACTGGGGCCAAGGACTTCGGTCACCGTCTCCTCAGGTGGTGGTGGTCTTGGCGGGCGGGCTCCGGTGGTGGTGGTCTTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGACCAACATCAACTGCAAGTCCAGCCAGAGTGTTTATAGACAGTCCACGAATAAGAACTCCTTAGCTTGGTACCAGCAGAAAACAGGACAGCTCTTAAATTAATCTTCTTCCCTGGGCATCTACGCGGAATCCGGGATCCCTGACCCGATTTCAGTGGCAGCGGGTCTGGGACAGATTTCACTCTCACTATTGACAGCCCGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTGTGCCACTTCCCGATCACCTTTGGCCAAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGTCCGAGGTGAGTGGTGGTGGTCTGAGTCTGAGGA GGATTGGTGCAGCTGGAGGGTCAATGAAAATCTCATGTGCAGCCTCTGGATTCACTTCAATAAGTAGCCCATGAACCTGGGTCCGCCAGGCTCCAGGAAAAGGTTTGGAAATGGGTTCGTGTCATAGAAGTAAAATAATAATAATAATGCAACATAATATGCCCAGATTAGTGAAAAGACAGGTTCACTATCTCCAGAGATGATTCAAAAAACACTGCCATATCTACAAAATGAACAACCTTGAAAACCTGAGGACACTGCCGTGTACTACTTGTGAGACATGGGAACTTCGGTAAATAGCTACATATCTACTTGGGCTTACTGGGGCCAAAGGACTCTGGTCAACCTTCAGTTGGTGGTGGTCTTGGCGGCGCGGCTCCGGTGGTGGTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGGAAACACTCACACTCACTTGTGGCTCCTCGACTGGGGCTGTACATCTGGCAACTACCCAACTGGGTCCAAACAAACCCAGGTCAGGCA CCCCCTGGTCTAATAGGTGGGACTAAGTTCCCTCGCCCCCGGTACTCCTGCCAGATTCTCAGGCTCC
224	SA08-CD33 E11 HL x I2C HL	nt	CAGGGCTGATCGCGCACATCTGCCTGCCCAGATGGGGCTGCCTGTGGGGCGACTCCCGTGAAACAGGTGTCAGCTGGTGACGCTGGAGCTGAGGTGAAGAGCCTGGAGAGTCAGTCAAGGTCTCCTGCAAGGCTAGCGGGTATACCTTCACAAAATATGGAATGAACTGGGTGAAAGCAGGCTCCAGGACAGGGTTTAGAGTGGGTGGATGATAAAACACCTACACTGGAGAGCCAACTATGCTGATAAGTTCCAGGGACGCGTTACCATGACTACGGATACCTCTACCAGCACTGCCCTATATGGAATAACCGCAACCTCGGAGGTGATGACCGCTGTATATTAATGTGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTGACTACTGGGGCCAAGGACTTCGGTCACCGTCTCCTCAGGTGGTGGTGGTCTTGGCGGGCGGGCTCCGGTGGTGGTGGTCTTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGACCAACATCAACTGCAAGTCCAGCCAGAGTGTTTATAGACAGTCCACGAATAAGAACTCCTTAGCTTGGTACCAGCAGAAAACAGGACAGCTCTTAAATTAATCTTCTTCCCTGGGCATCTACGCGGAATCCGGGATCCCTGACCCGATTTCAGTGGCAGCGGGTCTGGGACAGATTTCACTCTCACTATTGACAGCCCGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTGTGCCACTTCCCGATCACCTTTGGCCAAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGTCCGAGGTGAGTGGTGGTGGTCTGAGTCTGAGGA GGATTGGTGCAGCTGGAGGGTCAATGAAAATCTCATGTGCAGCCTCTGGATTCACTTCAATAAGTAGCCCATGAACCTGGGTCCGCCAGGCTCCAGGAAAAGGTTTGGAAATGGGTTCGTGTCATAGAAGTAAAATAATAATAATAATGCAACATAATATGCCCAGATTAGTGAAAAGACAGGTTCACTATCTCCAGAGATGATTCAAAAAACACTGCCATATCTACAAAATGAACAACCTTGAAAACCTGAGGACACTGCCGTGTACTACTTGTGAGACATGGGAACTTCGGTAAATAGCTACATATCTACTTGGGCTTACTGGGGCCAAAGGACTCTGGTCAACCTTCAGTTGGTGGTGGTCTTGGCGGCGCGGCTCCGGTGGTGGTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGGAAACACTCACACTCACTTGTGGCTCCTCGACTGGGGCTGTACATCTGGCAACTACCCAACTGGGTCCAAACAAACCCAGGTCAGGCA CCCCCTGGTCTAATAGGTGGGACTAAGTTCCCTCGCCCCCGGTACTCCTGCCAGATTCTCAGGCTCC

225	SA08-CD33 E11 HL x I2C HL		aa	CTGCTTGGAGGCAAGGCTGCCCTCACCCCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATATTAC TGTGTTCTATATGGTACAGCAACCGTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCTCTA QGLIGDIDLPRWGCLWGDVVKQVLVQSGAEVKKPGEVSVKVSCKASGYTFNNGMNVWVKQAPGQGL EWMGWINTYTGEPTYADKFQGRVTMTTDTSTSTAYMEIRNLGGDDTAVYCARWSWSDGYVYVFDY WGGTSTVTVSSGGGGSGGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSTNKNLSLA WYQOKPQPPKLLLSWASTRESGIPDRFSGSGSGTDFTLTIDSPQPEDSATYCYCQSAHFPIITFGQ GTRLEIKSGGGSEVQLVSESGGILVQPGSLKLSCAASGFTFNKYAMNVWRQAPGKGLEWVARIRS KYNNTATYADSVKDRFTISRDDSKNTAYLQMNLLKTEDTAVYCVVRHGNFNSYISYWAYWGQGT LVTVSSGGGGSGGGGSGTQVVTQEPSTLTVSPGGTFTLTTCGSSSTGAVTSGNYPNWVQOKPQQA PRGLIGGTFKFLAPGTPARFSGSLGGKAAATLSGVQVPEDEAEYCVLWVSNRWVFGGGTKLTIVL
226	CD33 E11 HL x I2C HL (His Tag)		nt	CAGGTGACGTGGTGCAGTCTGGAGCTGAGGTGAAGAAAGCTTGAGAGTCAGTCAAGGTCTCTCTGC AAGGTAGCGGGTATACCTTTCACAAAATATGGAATGAACTGGGTGAAGCAGGCTCCAGGACAGGGT TTAGAGTGGATGGGCTGGATAAAACACTACACTGGAGAGCAACCTATGCTGATAAGTTCCAGGGA CGGTTACCATGACTACGGATACCTCTACAGACACTGCCATATATGGAAAATCCGCAACCTCGGAGGT GATGACACGGCTGTATATTAATGTGCGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACTTTTGAC TACTGGGGCAAGGCACCTTCGGTACCGCTCTCTCAGGTGGTGGTGTTCGGCGGCGGCGGTCC GGTGGTGGTGTCTGACATCGTATGACACAGTCTCCAGACTCCCTGACTGTGTCTCTGGCGGAG AGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCACGAATAAGAACTCCCTTA GCTTGTACACAGCAAAAACAGGACAGCTCTCAAAATTAATCTCTTCTGGGCATCTACGCGGGA TCCGGGATCCCTGACCGATTCAGTGGCAGCGGTCTGGGACAGATTCACCTCTCACTATTGACAGC CCGAGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCACCTCCCGATCACTTTGGC CAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGCTCCGAGGTGACGTGGTCTGAGTCTGGA GGAGGATTGGTCAGCTGGAGGGTCAATTGAAAATCTCATGTGCAGCTCTGGATTCACTTCAAT AAGTACCCCATGAACTGGGTCGCCAGGCTCCAGGAAAAGGTTTGGAAATGGGTGCTCGCATAGA AGTAAATATAATTAATGCAACATATTAATGCCGATTCAAGTGAAGACAGGTTACCATCTCCAGA GATGATTCAAAAACACTGCCATCTACAAATGAACAACCTTGAAAACTGAGGACACTGCCGTGTAC TACTGTGTGAGACATGGGAACCTTCGGTAATAGCTACATATCTTACTGGCTTACTGGGCGCAAGGG ACTCTGGTCACCGTCTCCTCAGGTGGTGGTGTTCGGCGGCGGCGCTCCGGTGGTGGTGTCT CAGACTGTTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGGAAACAGTCACACTCACTGT GGCTCCTCGACTGGGGCTGTACATCTGGCAACTACCCAACTGGGTCCAAACCAACCAAGGTCCAG GCACCCCGTGGTCTAATAGGTGGACTAAGTTCCCTCGCCCCCGGTACTCTTCCAGATTCTCAGGC TCCCTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATAT TACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTCGGTGGAGGAACCAAACTGACTGTCTCTA CATCACCATCACCATCAC
227	CD33 E11 HL x I2C HL H6		aa	QVQLVQSGAEVKKPGEVSVKVSCKASGYTFNNGMNVWVKQAPGQGLQGLWGWINTYTGEPTYADKFQ RVMTTDTSTSTAYMEIRNLGGDDTAVYCARWSWSDGYVYVFDYWGQGTSTVTVSSGGGGSGGG GGGSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSTNKNLSLAWYQOKPQPPKLLLSWA STRESGIPDRFSGSGSGTDFTLTIDSPQPEDSATYCYCQSAHFPIITFGQGTREIKSGGGSEVQLV SESGGILVQPGSLKLSCAASGFTFNKYAMNVWRQAPGKGLEWVARIRSKYNNYATYADSVKDRFTISR

				DDSKNTAYLQMNILKTEDTAVYCVRHGNGNSYISYWAYWGQGTILTVSSGGGGGGGGGGGGGS QTVVTQEPSTLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGGKAALTLSGVQPEDEAFYCYCVLWYSNRWVFGGGTKLTVLHHHHHH
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eolf-seql
SEQUENCE LISTING

<110> Amgen Research (Munich) GmbH
Amgen Inc.

<120> Combination of epigenetic factors and bispecific compounds
targeting CD33 and CD3 in the treatment of myeloid leukemia

<130> AMG14853PCT

<150> US 61/877,714
<151> 2013-09-13

<160> 227

<170> PatentIn version 3.3

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35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Ser Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Glu Ile Asn Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
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Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp

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105

110

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 ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gccaacatat 180
 gctgatgact tcaagggacg gggtaccatg tcttcggata cctctaccag cactgcctat 240
 ttggaaatca acagcctcag aagtgatgac acggctatat attactgtgc gcgctggagt 300
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Ser Lys Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile
 50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr

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65	70	75	80
Ile Asp Ser Leu	Gln Pro Glu Asp Ser	Ala Thr Tyr Tyr Cys	Gln Gln
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Ser Ala His Phe	Pro Ile Thr Phe	Gly Gln Gly Thr Arg	Leu Glu Ile
	100	105	110

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tggtaccagc agaaaccagg acagcctcct aaattactcc tttcctgggc atctacgcgg 180

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35 40 45

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Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Ser Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Glu Ile Asn Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
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180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
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Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
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ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gccaacatat 180
gctgatgact tcaagggacg ggttaccatg tcttcggata cctctaccag cactgcctat 240
ttggaaatca acagcctcag aagtgatgac acggctatat attactgtgc gcgctggagt 300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg 420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
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20

25

30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Ser Ser Asp Thr Ser Thr Ser Thr Ala Tyr
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Leu Glu Ile Asn Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
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Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
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Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr

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Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys	Ser	Gly	Gly	Gly	Gly	Ser
				245					250					255	
Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
			260					265					270		
Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Lys	Tyr
		275					280					285			
Ala	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	290					295					300				
Ala	Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp
305					310					315					320
Ser	Val	Lys	Asp	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr
				325					330					335	
Ala	Tyr	Leu	Gln	Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr
			340					345					350		
Tyr	Cys	Val	Arg	His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Ile	Ser	Tyr	Trp
		355					360					365			
Ala	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly
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Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Thr	Val	Val
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Thr	Gln	Glu	Pro	Ser	Leu	Thr	Val	Ser	Pro	Gly	Gly	Thr	Val	Thr	Leu
				405					410					415	
Thr	Cys	Gly	Ser	Ser	Thr	Gly	Ala	Val	Thr	Ser	Gly	Tyr	Tyr	Pro	Asn
			420					425					430		
Trp	Val	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Gly	Leu	Ile	Gly	Gly

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435

440

445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
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Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
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Gly Gly Gly Thr Lys Leu Thr Val Leu
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gctgatgact tcaagggacg ggttaccatg tcttcggata cctctaccag cactgcctat 240
ttggaaatca acagcctcag aagtgatgac acggctatat attactgtgc gcgctggagt 300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
tcctcaggtg gtggtgggtc tggcggcggc ggctccgggtg gtggtgggtc tgacatcgtg 420
atgacacagt ctccagactc cctgactgtg tctctgggag agaggaccac catcaactgc 480
aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag 540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
atccctgacc gattcagtg cagcgggtct gggacagatt tcactctcac tattgacagc 660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720

eolf-seql

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tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg 780
gtcagagtctg gaggaggatt ggtgcagcct ggaggggtcat tgaaactctc atgtgcagcc 840
tctggattca ccttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt 900
ttggaatggg ttgctcgcac aagaagtaaa tataataatt atgcaacata ttatgccgat 960
tcagtgaaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080
ggtaatagct acatatccta ctgggcttac tggggccaag ggactctggt caccgtctcc 1140
tcagggtggtg gtggttctgg cggcggcggc tccgggtggtg gtggttctca gactgttgtg 1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
tcgactgggg ctgttacatc tggctactac ccaaactggg tccaacaaaa accaggtcag 1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
tcaggctccc tgcttgagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
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aaactgactg tccta 1515

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<210> 15
 <211> 505
 <212> PRT
 <213> artificial

<220>
 <223> CD33 AH3 HL x F12Q HL

<400> 15

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe

eolf-seql
50 55 60

Lys Gly Arg Val Thr Met Ser Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Glu Ile Asn Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

eolf-seql

260

265

270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
 355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
 385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
 405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
 420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
 435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
 450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp

		eolf-seql	
465	470	475	480

Glu	Ala	Glu	Tyr	Tyr	Cys	Val	Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe
				485					490					495	

Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu
			500					505

<210> 16
 <211> 1515
 <212> DNA
 <213> artificial

<220>
 <223> CD33 AH3 HL x F12Q HL

<400> 16
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 tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaggcaggct 120
 ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gccaacatat 180
 gctgatgact tcaagggacg ggttaccatg tcttcggata cctctaccag cactgcctat 240
 ttggaaatca acagcctcag aagtgatgac acggctatat attactgtgc gcgctggagt 300
 tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
 tcctcaggtg gtggtgggtc tggcggcggc ggctccgggtg gtggtgggtc tgacatcgtg 420
 atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
 aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag 540
 cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
 atccctgacc gattcagtgg cagcgggtct gggacagatt tcaactctac tattgacagc 660
 ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
 tttggccaag ggacacgact ggagattaaa tccggaggtg gtggctccga ggtgcagctg 780
 gtcgagtctg gaggaggatt ggtgcagcct ggaggggtcat tgaaactctc atgtgcagcc 840
 tctggattca ccttcaatag ctacgccatg aactgggtcc gccaggctcc aggaaagggt 900
 ttggaatggg ttgctcgcac aagaagtaaa tataataatt atgcaacata ttatgccgat 960

eolf-seql

tcagtgaag gcaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080
ggtaatagct acgtttcctg gtgggcttac tggggccaag ggactctggt caccgtctcc 1140
tcaggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctca gactgttgtg 1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
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gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
tcaggctccc tgcttgagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtttcgg tggaggaacc 1500
aaactgactg tccta 1515

<210> 17
<211> 505
<212> PRT
<213> artificial

<220>
<223> CD33 AH3 HL x I2C HL

<400> 17

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Ser Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Glu Ile Asn Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys

eolf-seql
90

85

95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

eolf-seql

290

295

300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu

<210> 18
 <211> 1515
 <212> DNA
 <213> artificial

<220>
 <223> CD33 AH3 HL x I2C HL

<400> 18
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 tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaggcaggct 120
 ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gccaacatat 180
 gctgatgact tcaagggacg ggttaccatg tcttcggata cctctaccag cactgcctat 240
 ttggaaatca acagcctcag aagtgatgac acggctatat attactgtgc gcgctggagt 300
 tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
 tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg 420
 atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
 aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag 540
 cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
 atccctgacc gattcagtggt cagcgggtct gggacagatt tcactctcac tattgacagc 660
 ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
 tttggccaag ggacacgact ggagattaaa tccggaggtg gtggctccga ggtgcagctg 780
 gtcgagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc 840
 tctggattca ctttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt 900
 ttggaatggg ttgctcgcac aagaagtaaa tataataatt atgcaacata ttatgccgat 960
 tcagtgaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
 atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080
 ggtaatagct acatatccta ctgggcttac tggggccaag ggactctggt caccgtctcc 1140
 tcaggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctca gactgttgtg 1200

eolf-seql

actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
 tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag 1320
 gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
 tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
 gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtgttcgg tggaggaacc 1500
 aaactgactg tccta 1515

<210> 19

<211> 122

<212> PRT

<213> artificial

<220>

<223> CD33 VH of AF5

<400> 19

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Leu Glu Leu His Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser

eolf-seql

115

120

<210> 20
<211> 5
<212> PRT
<213> artificial

<220>
<223> CD33 HCDR1 of AF5

<400> 20

Asn Tyr Gly Met Asn
1 5

<210> 21
<211> 17
<212> PRT
<213> artificial

<220>
<223> CD33 HCDR2 of AF5

<400> 21

Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe Lys
1 5 10 15

Gly

<210> 22
<211> 13
<212> PRT
<213> artificial

<220>
<223> CD33 HCDR3 of AF5

<400> 22

Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr
1 5 10

<210> 23
<211> 366
<212> DNA

eolf-seql

<213> artificial

<220>

<223> CD33 VH of AF5

<400> 23

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caggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagcgtc agtcaaggtc      60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct      120
ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat      180
gctgatgact tcaagggacg ggttaccatg acttcggata cctctaccag cactgcctat      240
ttggaactcc acaacctcag aagtgatgac acggctgtat attactgtgc gcgctggagt      300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc      360
tcctca                                          366
```

<210> 24

<211> 113

<212> PRT

<213> artificial

<220>

<223> CD33 VL of AF5

<400> 24

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Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Thr Val Ser Leu Gly
1           5           10          15
```

```
Glu Arg Thr Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser
          20           25          30
```

```
Ser Lys Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
          35           40          45
```

```
Pro Pro Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile
          50           55          60
```

```
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65           70           75          80
```

```
Ile Asp Ser Leu Gln Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln
```

85 eolf-seql 95
90

Ser Ala His Phe Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile
100 105 110

Lys

<210> 25
<211> 17
<212> PRT
<213> artificial

<220>
<223> CD33 LCDR1 of AF5

<400> 25

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
1 5 10 15

Ala

<210> 26
<211> 7
<212> PRT
<213> artificial

<220>
<223> CD33 LCDR2 of AF5

<400> 26

Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 27
<211> 9
<212> PRT
<213> artificial

<220>
<223> CD33 LCDR3 of AF5

<400> 27

eolf-seql

Gln Gln Ser Ala His Phe Pro Ile Thr
1 5

<210> 28
<211> 339
<212> DNA
<213> artificial

<220>
<223> CD33VL of AF5

<400> 28
gacatcgtga tgacacagtc tccagactcc ctgactgtgt ctctgggcga gaggaccacc 60
atcaactgca agtccagcca gagtgtttta gacagctcca agaataagaa ctccttagct 120
tggtaccagc agaaaccagg acagcctcct aaattactcc tttcctgggc atctacgcgg 180
gaatccggga tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcact 240
attgacagcc tgcagcctga agattctgca acttactatt gtcaacagtc tgcccacttc 300
ccgatcacct ttggccaagg gacacgactg gagattaaa 339

<210> 29
<211> 250
<212> PRT
<213> artificial

<220>
<223> CD33HL of AF5

<400> 29

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

eolf-seql

Lys Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Glu Leu His Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
245 250

<210> 30
<211> 750
<212> DNA

eolf-seql

<213> artificial

<220>

<223> CD33HL of AF5

<400> 30

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cagggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagcgtc agtcaaggtc      60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct      120
ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat      180
gctgatgact tcaaggagcg ggttaccatg acttcggata cctctaccag cactgcctat      240
ttggaactcc acaacctcag aagtgatgac acggctgtat attactgtgc gcgctggagt      300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc      360
tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg      420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc      480
aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag      540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg      600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc      660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc      720
tttggccaag ggacacgact ggagattaaa      750
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<210> 31

<211> 505

<212> PRT

<213> artificial

<220>

<223> CD33 AF5 HL x H2C HL

<400> 31

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10          15
```

```
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20           25           30
```

```
Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
```

eolf-seql

35

40

45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Glu Leu His Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser

eolf-seql
250

245

255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu

eolf-seql

450

455

460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 32

<211> 1515

<212> DNA

<213> artificial

<220>

<223> CD33 AF5 HL x H2C HL

<400> 32

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ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat	180
gctgatgact tcaagggacg ggttaccatg acttcggata cctctaccag cactgcctat	240
ttggaactcc acaacctcag aagtgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc	360
tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg	420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc	480
aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag	540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg	600
atccctgacc gattcagtg ggcgggtct gggacagatt tcactctcac tattgacagc	660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc	720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg	780
gtcgagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc	840

eolf-seq1

tctggattca ccttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaaggg 900
 ttggaatggg ttgctcgcat aagaagtaaa tataataatt atgcaacata ttatgccgat 960
 tcagtgaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
 atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080
 ggtaatagct acatatccta ctgggcttac tggggccaag ggactctggt caccgtctcc 1140
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 tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
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 aaactgactg tccta 1515

<210> 33
 <211> 505
 <212> PRT
 <213> artificial

<220>
 <223> CD33 AF5 HL x F12Q HL

<400> 33

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr

eolf-seql

65		70		75		80									
Leu	Glu	Leu	His	Asn	Leu	Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			85					90					95		
Ala	Arg	Trp	Ser	Trp	Ser	Asp	Gly	Tyr	Tyr	Val	Tyr	Phe	Asp	Tyr	Trp
			100					105					110		
Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly
		115					120					125			
Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Ile	Val	Met	Thr	Gln	Ser
	130					135					140				
Pro	Asp	Ser	Leu	Thr	Val	Ser	Leu	Gly	Glu	Arg	Thr	Thr	Ile	Asn	Cys
145					150					155					160
Lys	Ser	Ser	Gln	Ser	Val	Leu	Asp	Ser	Ser	Lys	Asn	Lys	Asn	Ser	Leu
			165						170					175	
Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	Lys	Leu	Leu	Leu	Ser
			180					185					190		
Trp	Ala	Ser	Thr	Arg	Glu	Ser	Gly	Ile	Pro	Asp	Arg	Phe	Ser	Gly	Ser
		195					200					205			
Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asp	Ser	Leu	Gln	Pro	Glu
	210						215				220				
Asp	Ser	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Ala	His	Phe	Pro	Ile	Thr
225					230					235					240
Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys	Ser	Gly	Gly	Gly	Gly	Ser
			245						250					255	
Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
		260						265					270		
Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Ser	Tyr

eolf-seql

275

280

285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe

485 eolf-seql 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 34
<211> 1515
<212> DNA
<213> artificial

<220>
<223> CD33 AF5 HL x F12Q HL

<400> 34
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ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat 180
gctgatgact tcaaggagc gggtaccatg acttcggata cctctaccag cactgcctat 240
ttggaactcc acaacctcag aagtgatgac acggctgtat attactgtgc gcgctggagt 300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
tcctcaggtg gtggtgggtc tggcggcggc ggctccggtg gtggtgggtc tgacatcgtg 420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag 540
cagaaaccag gacagcctcc taaattactc ctttctggg catctacgcg ggaatccggg 600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc 660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg 780
gtcgagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc 840
tctggattca cttcaatag ctacgccatg aactgggtcc gccaggctcc aggaaagggt 900
ttggaatggg ttgctcgcag aagaagtaaa tataataatt atgcaacata ttatgccgat 960
tcagtgaaag gcaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080

eolf-seql

ggtaatagct acgtttcctg gtgggcttac tggggccaag ggactctggt caccgtctcc 1140
tcaggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctca gactgttgtg 1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag 1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
tcaggctccc tgcttgagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtgttcgg tggaggaacc 1500
aaactgactg tccta 1515

<210> 35
<211> 505
<212> PRT
<213> artificial

<220>
<223> CD33 AF5 HL x I2C HL

<400> 35

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Glu Leu His Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp

eolf-seql

100

105

110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
 130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
 165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
 180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
 210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
 225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp

eolf-seql																		
305						310						315						320
Ser	Val	Lys	Asp	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr			
				325					330					335				
Ala	Tyr	Leu	Gln	Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr			
			340					345					350					
Tyr	Cys	Val	Arg	His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Ile	Ser	Tyr	Trp			
		355					360					365						
Ala	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly			
	370					375					380							
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Thr	Val	Val			
385					390					395					400			
Thr	Gln	Glu	Pro	Ser	Leu	Thr	Val	Ser	Pro	Gly	Gly	Thr	Val	Thr	Leu			
				405					410					415				
Thr	Cys	Gly	Ser	Ser	Thr	Gly	Ala	Val	Thr	Ser	Gly	Asn	Tyr	Pro	Asn			
			420					425					430					
Trp	Val	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Gly	Leu	Ile	Gly	Gly			
		435					440					445						
Thr	Lys	Phe	Leu	Ala	Pro	Gly	Thr	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu			
	450					455					460							
Leu	Gly	Gly	Lys	Ala	Ala	Leu	Thr	Leu	Ser	Gly	Val	Gln	Pro	Glu	Asp			
465					470					475					480			
Glu	Ala	Glu	Tyr	Tyr	Cys	Val	Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe			
				485					490					495				
Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu										
			500					505										

<210> 36

eolf-seql

<211> 1515

<212> DNA

<213> artificial

<220>

<223> CD33 AF5 HL x I2C HL

<400> 36

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tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct	120
ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat	180
gctgatgact tcaagggacg ggttaccatg acttcggata cctctaccag cactgcctat	240
ttggaactcc acaacctcag aagtgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc	360
tcctcagggtg gtggtggttc tggcggcggc ggctccgggtg gtggtggttc tgacatcgtg	420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc	480
aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag	540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg	600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc	660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc	720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg	780
gtcagagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc	840
tctggattca cttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt	900
ttggaatggg ttgctcgcat aagaagtaaa tataataatt atgcaacata ttatgccgat	960
tcagtgaaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa	1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc	1080
ggtaatagct acatatccta ctgggcttac tggggccaag ggactctgggt caccgtctcc	1140
tcaggtggtg gtggttcttg cggcggcggc tccgggtggtg gtggttctca gactgttgtg	1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc	1260
tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag	1320

eolf-seql

gcaccccgctg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
 tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
 gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtgttcgg tggaggaacc 1500
 aaactgactg tccta 1515

<210> 37
 <211> 122
 <212> PRT
 <213> artificial

<220>
 <223> CD33 VH of AC8

<400> 37

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Ile Arg Asn Leu Arg Asn Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 38

eolf-seql

<211> 5
 <212> PRT
 <213> artificial

<220>
 <223> CD33 HCDR1 of AC8

<400> 38

Asn Tyr Gly Met Asn
 1 5

<210> 39
 <211> 17
 <212> PRT
 <213> artificial

<220>
 <223> CD33 HCDR2 of AC8

<400> 39

Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe Lys
 1 5 10 15

Gly

<210> 40
 <211> 13
 <212> PRT
 <213> artificial

<220>
 <223> CD33 HCDR3 of AC8

<400> 40

Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr
 1 5 10

<210> 41
 <211> 366
 <212> DNA
 <213> artificial

<220>
 <223> CD33 VH of AC8

eolf-seql

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<400> 41
caggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggtc      60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct      120
ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat      180
gctgatgact tcaagggacg ggttaccatg actacggata cctctaccag cactgcctat      240
atggaaatcc gcaacctcag aaatgatgac acggctgtat attactgtgc gcgctggagt      300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc      360
tcctca                                          366

```

```

<210> 42
<211> 113
<212> PRT
<213> artificial

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```

<220>
<223> CD33 VL of AC8

```

```

<400> 42

```

```

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Thr Val Ser Leu Gly
1           5           10          15

```

```

Glu Arg Thr Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser
          20           25          30

```

```

Ser Lys Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
          35           40          45

```

```

Pro Pro Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile
          50           55          60

```

```

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65           70           75          80

```

```

Ile Asp Ser Leu Gln Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln
          85           90          95

```

```

Ser Ala His Phe Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile

```


eolf-seql

100

105

110

Lys

<210> 43

<211> 17

<212> PRT

<213> artificial

<220>

<223> CD33 LCDR1 of AC8

<400> 43

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
 1 5 10 15

Ala

<210> 44

<211> 7

<212> PRT

<213> artificial

<220>

<223> CD33 LCDR2 of AC8

<400> 44

Trp Ala Ser Thr Arg Glu Ser
 1 5

<210> 45

<211> 9

<212> PRT

<213> artificial

<220>

<223> CD33 LCDR3 of AC8

<400> 45

Gln Gln Ser Ala His Phe Pro Ile Thr
 1 5

eolf-seql

<210> 46
 <211> 339
 <212> DNA
 <213> artificial

<220>
 <223> CD33 VL of AC8

<400> 46
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 atcaactgca agtccagcca gagtgtttta gacagctcca agaataagaa ctccttagct 120
 tgggtaccagc agaaaccagg acagcctcct aaattactcc tttcctgggc atctacgcgg 180
 gaatccggga tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcact 240
 attgacagcc tgcagcctga agattctgca acttactatt gtcaacagtc tgcccacttc 300
 ccgatcacct ttggccaagg gacacgactg gagattaaa 339

<210> 47
 <211> 250
 <212> PRT
 <213> artificial

<220>
 <223> CD33 HL of AC8

<400> 47

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

eolf-seql

Met Glu Ile Arg Asn Leu Arg Asn Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
245 250

<210> 48

<211> 750

<212> DNA

<213> artificial

<220>

<223> CD33 HL of AC8

eolf-seql

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<400> 48
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tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct      120
ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat      180
gctgatgact tcaagggacg ggttaccatg actacggata cctctaccag cactgcctat      240
atggaaatcc gcaacctcag aaatgatgac acggctgtat attactgtgc gcgctggagt      300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc      360
tcctcagggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg      420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc      480
aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag      540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg      600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc      660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc      720
tttggccaag ggacacgact ggagattaataa                                     750

```

```

<210> 49
<211> 505
<212> PRT
<213> artificial

```

```

<220>
<223> CD33 AC8 HL x H2C HL

```

```

<400> 49

```

```

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1           5           10           15

```

```

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20           25           30

```

```

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35           40           45

```

```

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe

```

eolf-seql
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Arg Asn Leu Arg Asn Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

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260

265

270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
 355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
 385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
 405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
 420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
 435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
 450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp

465	470	eolf-seql 475	480
-----	-----	------------------	-----

Glu	Ala	Glu	Tyr	Tyr	Cys	Ala	Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe
				485					490					495	

Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu
			500					505

<210> 50
 <211> 1515
 <212> DNA
 <213> artificial

<220>
 <223> CD33 AC8 HL x H2C HL

<400> 50
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 ccaggacagg gtttaaagtg gatgggctgg ataaacacct acactggaga gccaacatat 180
 gctgatgact tcaagggacg ggttaccatg actacggata cctctaccag cactgcctat 240
 atggaaatcc gcaacctcag aaatgatgac acggctgtat attactgtgc gcgctggagt 300
 tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
 tcctcagggtg gtggtgggttc tggcggcggc ggctccgggtg gtggtgggtc tgacatcgtg 420
 atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
 aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag 540
 cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
 atccctgacc gattcagtgg cagcgggtct gggacagatt tcaactctac tattgacagc 660
 ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
 tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg 780
 gtcgagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc 840
 tctggattca ccttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt 900
 ttggaatggg ttgctcgcac aagaagtaaa tataataatt atgcaacata ttatgccgat 960

eolf-seql

tcagtgaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080
ggtaatagct acatatccta ctgggcttac tggggccaag ggactctggt caccgtctcc 1140
tcaggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctca gactgttgtg 1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
tcgactgggg ctgttacatc tggctactac ccaaactggg tccaacaaaa accaggtcag 1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
tcaggctccc tgcttgagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
gaggcagaat attactgtgc tctatggtac agcaaccgct ggggtgttcgg tggaggaacc 1500
aaactgactg tccta 1515

<210> 51
<211> 505
<212> PRT
<213> artificial

<220>
<223> CD33 AC8 HL x F12Q HL

<400> 51

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Arg Asn Leu Arg Asn Asp Asp Thr Ala Val Tyr Tyr Cys

eolf-seql
90

85

95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

eolf-seql

290

295

300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu

<210> 52
 <211> 1515
 <212> DNA
 <213> artificial

<220>
 <223> CD33 AC8 HL x F12Q HL

<400> 52
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 tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120
 ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat 180
 gctgatgact tcaagggacg ggttaccatg actacggata cctctaccag cactgcctat 240
 atggaaatcc gcaacctcag aaatgatgac acggctgtat attactgtgc gcgctggagt 300
 tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
 tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg 420
 atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
 aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag 540
 cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
 atccctgacc gattcagtggt cagcgggtct gggacagatt tcactctcac tattgacagc 660
 ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
 tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg 780
 gtcgagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc 840
 tctggattca ctttcaatag ctacgccatg aactgggtcc gccaggctcc aggaaagggt 900
 ttggaatggg ttgctcgcac aagaagtaaa tataataatt atgcaacata ttatgccgat 960
 tcagtgaag gcaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
 atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080
 ggtaatagct acgtttcctg gtgggcttac tggggccaag ggactctggt caccgtctcc 1140
 tcaggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctca gactgttgtg 1200

eolf-seql

actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
 tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag 1320
 gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
 tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
 gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtgttcgg tggaggaacc 1500
 aaactgactg tccta 1515

<210> 53

<211> 505

<212> PRT

<213> artificial

<220>

<223> CD33 AC8 HL x I2C HL

<400> 53

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Ile Arg Asn Leu Arg Asn Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly

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115

120

125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr

eolf-seql
330

325

335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 54
<211> 1515
<212> DNA
<213> artificial

eolf-seql

<220>

<223> CD33 AC8 HL x I2C HL

<400> 54

caggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggct	60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct	120
ccaggacagg gtttaaagtg gatgggctgg ataaacacct acactggaga gccaacatat	180
gctgatgact tcaagggacg ggttaccatg actacggata cctctaccag cactgcctat	240
atggaaatcc gcaacctcag aaatgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc	360
tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg	420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc	480
aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag	540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg	600
atccctgacc gattcagtggt cagcgggtct gggacagatt tcactctcac tattgacagc	660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc	720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg	780
gtcagagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaaactctc atgtgcagcc	840
tctggattca cttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt	900
ttggaatggg ttgctcgcgcat aagaagtaaa tataataatt atgcaacata ttatgccgat	960
tcagtgaaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa	1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc	1080
ggtaatagct acatatccta ctgggcttac tggggccaag ggactctggt caccgtctcc	1140
tcaggtggtg gtggttcttg cggcggcggc tccggtggtg gtggttctca gactgttggtg	1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc	1260
tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag	1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc	1380
tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat	1440

eolf-seql

gaggcagaat attactgtgt tctatggtag agcaaccgct ggggtgttcgg tggaggaacc 1500

aaactgactg tccta 1515

<210> 55

<211> 122

<212> PRT

<213> artificial

<220>

<223> CD33 VH of AH11

<400> 55

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Ser Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 56

<211> 5

<212> PRT

<213> artificial

eolf-seql

<220>

<223> CD33 HCDR1 of AH11

<400> 56

Asn Tyr Gly Met Asn

1 5

<210> 57

<211> 17

<212> PRT

<213> artificial

<220>

<223> CD33 HCDR2 of AH11

<400> 57

Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe Lys

1 5 10 15

Gly

<210> 58

<211> 13

<212> PRT

<213> artificial

<220>

<223> HCDR3

<400> 58

Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr

1 5 10

<210> 59

<211> 366

<212> DNA

<213> artificial

<220>

<223> CD33 VH of AH11

<400> 59

caggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggtc 60

eolf-seql

tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct	120
ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat	180
gctgatgact tcaagggacg ggttaccatg acttcggata cctctaccag cactgcctat	240
atggaaatca gcagcctcag aagtgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc	360
tcctca	366

<210> 60

<211> 113

<212> PRT

<213> artificial

<220>

<223> CD33 VL of AH11

<400> 60

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Asp	Ser	Leu	Thr	Val	Ser	Leu	Gly
1				5				10					15		

Glu	Arg	Thr	Thr	Ile	Asn	Cys	Lys	Ser	Ser	Gln	Ser	Val	Leu	Asp	Ser
		20					25						30		

Ser	Lys	Asn	Lys	Asn	Ser	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln
	35					40					45				

Pro	Pro	Lys	Leu	Leu	Leu	Ser	Trp	Ala	Ser	Thr	Arg	Glu	Ser	Gly	Ile
	50					55					60				

Pro	Asp	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr
65					70					75				80	

Ile	Asp	Ser	Leu	Gln	Pro	Glu	Asp	Ser	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln
			85						90					95	

Ser	Ala	His	Phe	Pro	Ile	Thr	Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile
			100					105					110		

Lys

eolf-seql

<210> 61
<211> 17
<212> PRT
<213> artificial

<220>
<223> CD33 LCDR1 of AH11

<400> 61

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
1 5 10 15

Ala

<210> 62
<211> 7
<212> PRT
<213> artificial

<220>
<223> CD33 LCDR2 of AH11

<400> 62

Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 63
<211> 9
<212> PRT
<213> artificial

<220>
<223> CD33LCDR3 of AH11

<400> 63

Gln Gln Ser Ala His Phe Pro Ile Thr
1 5

<210> 64
<211> 339
<212> DNA

eolf-seql

<213> artificial

<220>

<223> CD33 VL of AH11

<400> 64

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gacatcgtga tgacacagtc tccagactcc ctgactgtgt ctctgggcga gaggaccacc      60
atcaactgca agtccagcca gagtgtttta gacagctcca agaataagaa ctccttagct      120
tggtaccagc agaaaccagg acagcctcct aaattactcc tttcctgggc atctacgcgg      180
gaatccggga tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcact      240
attgacagcc tgcagcctga agattctgca acttactatt gtcaacagtc tgcccacttc      300
ccgatcacct ttggccaagg gacacgactg gagattaaa                                339

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<210> 65

<211> 250

<212> PRT

<213> artificial

<220>

<223> CD33 HL of AH11

<400> 65

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1           5           10          15

```

```

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
          20          25          30

```

```

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
          35          40          45

```

```

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
          50          55          60

```

```

Lys Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
          65          70          75          80

```

```

Met Glu Ile Ser Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
          85          90          95

```

eolf-seql

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
 130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
 165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
 180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
 210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
 225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
 245 250

<210> 66

<211> 750

<212> DNA

<213> artificial

<220>

<223> CD33 HL of AH11

<400> 66

cagggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggtc

60

eolf-seql

tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120
ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat 180
gctgatgact tcaagggacg ggttaccatg acttcggata cctctaccag cactgcctat 240
atggaaatca gcagcctcag aagtgatgac acggctgtat attactgtgc gcgctggagt 300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg 420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag 540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc 660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
tttggccaag ggacacgact ggagattaaa 750

<210> 67
<211> 505
<212> PRT
<213> artificial

<220>
<223> CD33 AH11 HL x H2C HL

<400> 67

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr

eolf-seql

65		70		75		80									
Met	Glu	Ile	Ser	Ser	Leu	Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			85					90					95		
Ala	Arg	Trp	Ser	Trp	Ser	Asp	Gly	Tyr	Tyr	Val	Tyr	Phe	Asp	Tyr	Trp
			100					105					110		
Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly
		115					120					125			
Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Ile	Val	Met	Thr	Gln	Ser
	130					135					140				
Pro	Asp	Ser	Leu	Thr	Val	Ser	Leu	Gly	Glu	Arg	Thr	Thr	Ile	Asn	Cys
145					150					155					160
Lys	Ser	Ser	Gln	Ser	Val	Leu	Asp	Ser	Ser	Lys	Asn	Lys	Asn	Ser	Leu
			165						170					175	
Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	Lys	Leu	Leu	Leu	Ser
			180					185					190		
Trp	Ala	Ser	Thr	Arg	Glu	Ser	Gly	Ile	Pro	Asp	Arg	Phe	Ser	Gly	Ser
	195						200					205			
Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asp	Ser	Leu	Gln	Pro	Glu
	210						215				220				
Asp	Ser	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Ala	His	Phe	Pro	Ile	Thr
225					230					235					240
Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys	Ser	Gly	Gly	Gly	Gly	Ser
			245						250					255	
Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
		260						265					270		
Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Lys	Tyr

eolf-seql

275

280

285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
 355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
 385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
 405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
 420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
 435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
 450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
 465 470 475 480

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe

485 eolf-seql 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 68
<211> 1515
<212> DNA
<213> artificial

<220>
<223> CD33 AH11 HL x H2C HL

<400> 68
caggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggct 60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120
ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat 180
gctgatgact tcaagggacg ggttaccatg acttcggata cctctaccag cactgcctat 240
atggaaatca gcagcctcag aagtgatgac acggctgtat attactgtgc gcgctggagt 300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
tcctcaggtg gtggtgggtc tggcggcggc ggctccggtg gtggtgggtc tgacatcgtg 420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag 540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc 660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg 780
gtcgagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc 840
tctggattca cttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt 900
ttggaatggg ttgctcgcat aagaagtaaa tataataatt atgcaacata ttatgccgat 960
tcagtgaaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080

eolf-seql

ggtaatagct acatataccta ctgggcttac tggggccaag ggactctggt caccgtctcc 1140
tcaggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctca gactgttgtg 1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
tcgactgggg ctgttacatc tggctactac ccaaactggg tccaacaaaa accaggtcag 1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
tcaggctccc tgcttgagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
gaggcagaat attactgtgc tctatggtac agcaaccgct ggggtgttcgg tggaggaacc 1500
aaactgactg tccta 1515

<210> 69
<211> 505
<212> PRT
<213> artificial

<220>
<223> CD33 AH11 HL x F12Q HL

<400> 69

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Ser Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp

eolf-seql

100

105

110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
 130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
 165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
 180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
 210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
 225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp

eolf-seql																
305				310				315				320				
Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr	
				325					330					335		
Ala	Tyr	Leu	Gln	Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr	
				340					345					350		
Tyr	Cys	Val	Arg	His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Val	Ser	Trp	Trp	
				355					360					365		
Ala	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	
				370					375					380		
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Thr	Val	Val	
				385					390					395		
Thr	Gln	Glu	Pro	Ser	Leu	Thr	Val	Ser	Pro	Gly	Gly	Thr	Val	Thr	Leu	
				405					410					415		
Thr	Cys	Gly	Ser	Ser	Thr	Gly	Ala	Val	Thr	Ser	Gly	Asn	Tyr	Pro	Asn	
				420					425					430		
Trp	Val	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Gly	Leu	Ile	Gly	Gly	
				435					440					445		
Thr	Lys	Phe	Leu	Ala	Pro	Gly	Thr	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu	
				450					455					460		
Leu	Gly	Gly	Lys	Ala	Ala	Leu	Thr	Leu	Ser	Gly	Val	Gln	Pro	Glu	Asp	
				465					470					475		
Glu	Ala	Glu	Tyr	Tyr	Cys	Val	Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe	
				485					490					495		
Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu								
				500					505							

eolf-seql

<211> 1515
 <212> DNA
 <213> artificial

<220>
 <223> CD33 AH11 HL x F12Q HL

<400> 70
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 ccaggacagg gtttaaagtg gatgggctgg ataaacacct aactggaga gccaacatat 180
 gctgatgact tcaagggacg ggttaccatg acttcggata cctctaccag cactgcctat 240
 atggaaatca gcagcctcag aagtgatgac acggctgtat attactgtgc gcgctggagt 300
 tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
 tcctcagggtg gtggtggttc tggcggcggc ggctccgggtg gtggtggttc tgacatcgtg 420
 atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
 aagtccagcc agagtgtttt agacagctcc aagaataaga actccttagc ttggtaccag 540
 cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
 atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc 660
 ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
 tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg 780
 gtcgagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc 840
 tctggattca cttcaatag ctacgccatg aactgggtcc gccaggctcc aggaaagggt 900
 ttggaatggg ttgctcgcat aagaagtaaa tataataatt atgcaacata ttatgccgat 960
 tcagtgaaag gcaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
 atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080
 ggtaatagct acgtttcctg gtgggcttac tggggccaag ggactctggt caccgtctcc 1140
 tcaggtggtg gtggttcttg cggcggcggc tccgggtggtg gtggttctca gactgttgtg 1200
 actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
 tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag 1320

eolf-seql

gcaccccgctg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
 tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
 gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtgttcgg tggaggaacc 1500
 aaactgactg tccta 1515

<210> 71
 <211> 505
 <212> PRT
 <213> artificial

<220>
 <223> CD33 AH11 HL x I2C HL

<400> 71

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Ile Ser Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser

eolf-seql

130

135

140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu
 165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
 180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
 210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
 225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr

eolf-seql

340

345

350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
 355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
 385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
 405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
 420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
 435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
 450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
 465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
 485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
 500 505

<210> 72

<211> 1515

<212> DNA

<213> artificial

<220>

<223> CD33 AH11 HL x I2C HL

<400> 72

eolf-seql

caggtgcagc	tggtgcagtc	tgagagctgag	gtgaagaagc	ctggagagtc	agtcaaggtc	60
tcctgcaagg	ctagcgggta	taccttcaca	aactatggaa	tgaactgggt	gaagcaggct	120
ccaggacagg	gtttaaagt	gatgggctgg	ataaacacct	acactggaga	gccaacatat	180
gctgatgact	tcaagggacg	ggttaccatg	acttcggata	cctctaccag	cactgcctat	240
atggaaatca	gcagcctcag	aagtgatgac	acggctgtat	attactgtgc	gcgctggagt	300
tgagtgatg	gttactacgt	ttactttgac	tactggggcc	aaggcactac	ggtcaccgtc	360
tcctcaggtg	gtggtggttc	tggcggcggc	ggctccggtg	gtggtggttc	tgacatcgtg	420
atgacacagt	ctccagactc	cctgactgtg	tctctgggcg	agaggaccac	catcaactgc	480
aagtccagcc	agagtgtttt	agacagctcc	aagaataaga	actccttagc	ttggtaccag	540
cagaaaccag	gacagcctcc	taaattactc	ctttcctggg	catctacgcg	ggaatccggg	600
atccctgacc	gattcagtgg	cagcgggtct	gggacagatt	tcactctcac	tattgacagc	660
ctgcagcctg	aagattctgc	aacttactat	tgtcaacagt	ctgcccactt	cccgatcacc	720
tttggccaag	ggacacgact	ggagattaaa	tccggagggtg	gtggctccga	ggtgcagctg	780
gtcgagtctg	gaggaggatt	ggtgcagcct	ggagggtcat	tgaaactctc	atgtgcagcc	840
tctggattca	ccttcaataa	gtacgccatg	aactgggtcc	gccaggctcc	aggaaagggt	900
ttggaatggg	ttgctcgcac	aagaagtaaa	tataataatt	atgcaacata	ttatgccgat	960
tcagtgaaag	acaggttcac	catctccaga	gatgattcaa	aaaacactgc	ctatctacaa	1020
atgaacaact	tgaaaactga	ggacactgcc	gtgtactact	gtgtgagaca	tgggaacttc	1080
ggtaatagct	acatatccta	ctgggcttac	tggggccaag	ggactctggt	caccgtctcc	1140
tcaggtgggtg	gtggttctgg	cggcggcggc	tccggtgggtg	gtggttctca	gactgttgtg	1200
actcaggaac	cttcactcac	cgtatcacct	ggtggaacag	tcacactcac	ttgtggctcc	1260
tcgactgggg	ctgttacatc	tggcaactac	ccaaactggg	tccaacaaaa	accaggtcag	1320
gcaccccgtg	gtctaatagg	tgggactaag	ttcctcgccc	ccggtactcc	tgccagattc	1380
tcaggctccc	tgcttggagg	caaggctgcc	ctcaccctct	caggggtaca	gccagaggat	1440
gaggcagaat	attactgtgt	tctatggtac	agcaaccgct	gggtgttcgg	tggaggaacc	1500
aaactgactg	tccta					1515

eolf-seql

<210> 73
 <211> 122
 <212> PRT
 <213> artificial

<220>
 <223> CD33 VH of B3

<400> 73

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe
 50 55 60

Gln Gly Arg Val Thr Phe Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Asn Leu Lys Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 74
 <211> 5
 <212> PRT
 <213> artificial

<220>
 <223> CD33 HCDR1 of B3

<400> 74

eolf-seql

Asn Tyr Gly Met Asn
1 5

<210> 75
<211> 17
<212> PRT
<213> artificial

<220>
<223> CD33 HCDR2 of B3

<400> 75

Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe Gln
1 5 10 15

Gly

<210> 76
<211> 13
<212> PRT
<213> artificial

<220>
<223> CD33 HCDR3 of B3

<400> 76

Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr
1 5 10

<210> 77
<211> 366
<212> DNA
<213> artificial

<220>
<223> CD33 VH of B3

<400> 77
caggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggct 60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120
ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gacaaactat 180

eolf-seql

gctgataagt tccagggacg cgttaccttc acttcggata cctctaccag cactgcctat 240
atggaactcc gcaacctcaa aagtgatgac acggctgtat attactgtgc gcgctggagt 300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
tcctca 366

<210> 78
<211> 113
<212> PRT
<213> artificial

<220>
<223> CD33 VL of B3

<400> 78

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Met Thr Val Ser Leu Gly
1 5 10 15

Glu Arg Thr Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser
20 25 30

Ser Thr Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Asp Ser Leu Gln Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln
85 90 95

Ser Ala His Phe Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Asp Ile
100 105 110

Lys

<210> 79

eolf-seql

<211> 17
 <212> PRT
 <213> artificial

<220>
 <223> CD33 LCDR1 of B3

<400> 79

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
 1 5 10 15

Ala

<210> 80
 <211> 6
 <212> PRT
 <213> artificial

<220>
 <223> CD33 LCDR2 of B3

<400> 80

Trp Ala Ser Thr Arg Glu
 1 5

<210> 81
 <211> 9
 <212> PRT
 <213> artificial

<220>
 <223> CD33LCDR3 of B3

<400> 81

Gln Gln Ser Ala His Phe Pro Ile Thr
 1 5

<210> 82
 <211> 339
 <212> DNA
 <213> artificial

<220>
 <223> CD33 VL of B3

eolf-seql

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<400> 82
gacatcgtga tgacacagtc tccagactcc atgactgtgt ctctgggcga gaggaccacc      60
atcaactgca agtccagcca gagtgtttta gacagctcca cgaataagaa ctccttagct      120
tggtaccagc agaaaccagg acagcctcct aaattactcc tttcctgggc atctacgcgg      180
gaatccggga tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcact      240
attgacagcc tgcagcctga agattctgca acttactatt gtcaacagtc tgcccacttc      300
ccgatcacct ttggccaagg gacacgactg gacattaaa                                339

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<210> 83
<211> 250
<212> PRT
<213> artificial

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<220>
<223> CD33 HL of B3

```

```

<400> 83

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1          5          10          15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
          20          25          30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
          35          40          45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe
50          55          60

Gln Gly Arg Val Thr Phe Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65          70          75          80

Met Glu Leu Arg Asn Leu Lys Ser Asp Asp Thr Ala Val Tyr Tyr Cys
          85          90          95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100         105         110

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eolf-seql

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Met Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Asp Ile Lys
245 250

<210> 84
<211> 750
<212> DNA
<213> artificial

<220>
<223> CD33 HL of B3

<400> 84
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tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120
ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gacaaactat 180

eolf-seql

gctgataagt tccagggacg cgttaccttc acttcggata cctctaccag cactgcctat 240
atggaactcc gcaacctcaa aagtgatgac acggctgtat attactgtgc gcgctggagt 300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
tcctcaggtg gtggtgggtc tggcggcggc ggctccggtg gtggtgggtc tgacatcgtg 420
atgacacagt ctccagactc catgactgtg tctctgggcg agaggaccac catcaactgc 480
aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag 540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
atccctgacc gattcagtg gacgggtct gggacagatt tcactctcac tattgacagc 660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
tttggccaag ggacacgact ggacattaaa 750

<210> 85
<211> 505
<212> PRT
<213> artificial

<220>
<223> CD33 B3 HL x H2C HL

<400> 85

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Phe Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Asn Leu Lys Ser Asp Asp Thr Ala Val Tyr Tyr Cys

eolf-seql
90

85

95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Met Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Asp Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

eolf-seql

290

295

300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
 355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
 385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
 405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
 420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
 435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
 450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
 465 470 475 480

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
 485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu

500

505

<210> 86
 <211> 1515
 <212> DNA
 <213> artificial

<220>
 <223> CD33 B3 HL x H2C HL

<400> 86
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 ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gacaaactat 180
 gctgataagt tccagggacg cgttaccttc acttcggata cctctaccag cactgcctat 240
 atggaactcc gcaacctcaa aagtgatgac acggctgtat attactgtgc gcgctggagt 300
 tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
 tcctcaggtg gtggtgggtc tggcggcggc ggctccgggtg gtggtgggtc tgacatcgtg 420
 atgacacagt ctccagactc catgactgtg tctctgggcg agaggaccac catcaactgc 480
 aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag 540
 cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
 atccctgacc gattcagtggt cagcgggtct gggacagatt tcactctcac tattgacagc 660
 ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
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 gtcgagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc 840
 tctggattca ctttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt 900
 ttggaatggg ttgctcgcac aagaagtaaa tataataatt atgcaacata ttatgccgat 960
 tcagtgaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
 atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080
 ggtaatagct acatattcta ctgggcttac tggggccaag ggactctggt caccgtctcc 1140
 tcaggtgggtg gtggttctgg cggcggcggc tccggtgggtg gtggttctca gactgttgtg 1200

eolf-seql

actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
 tcgactgggg ctgttacatc tggctactac ccaaactggg tccaacaaaa accaggtcag 1320
 gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
 tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
 gaggcagaat attactgtgc tctatggtac agcaaccgct ggggtgttcgg tggaggaacc 1500
 aaactgactg tccta 1515

<210> 87
 <211> 505
 <212> PRT
 <213> artificial

<220>
 <223> CD33 B3 HL x F12Q HL

<400> 87

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe
 50 55 60

Gln Gly Arg Val Thr Phe Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Asn Leu Lys Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly

eolf-seql

115

120

125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
 130 135 140

Pro Asp Ser Met Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
 165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
 180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
 210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
 225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Asp Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr

eolf-seql
330

325

335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 88
<211> 1515
<212> DNA
<213> artificial

eolf-seql

<220>

<223> CD33 B3 HL x F12Q HL

<400> 88

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ccaggacagg gtttagagtg gatgggctgg ataaacacct acactggaga gacaaactat	180
gctgataagt tccaggggacg cgttaccttc acttcggata cctctaccag cactgcctat	240
atggaactcc gcaacctcaa aagtgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc	360
tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg	420
atgacacagt ctccagactc catgactgtg tctctgggcg agaggaccac catcaactgc	480
aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag	540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg	600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc	660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc	720
tttggccaag ggacacgact ggacattaaa tccggagggtg gtggctccga ggtgcagctg	780
gtcagagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaaactctc atgtgcagcc	840
tctggattca ctttcaatag ctacgccatg aactgggtcc gccaggctcc aggaaaggggt	900
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tcagtgaaag gcaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa	1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc	1080
ggtaatagct acgtttcctg gtgggcttac tggggccaag ggactctggt caccgtctcc	1140
tcaggtggtg gtggttcttg cggcggcggc tccggtggtg gtggttctca gactgttggtg	1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc	1260
tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag	1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc	1380
tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat	1440

eolf-seql

gaggcagaat attactgtgt tctatgggtac agcaaccgct ggggtgttcgg tggaggaacc 1500

aaactgactg tccta 1515

<210> 89

<211> 505

<212> PRT

<213> artificial

<220>

<223> CD33 B3 HL x I2C HL

<400> 89

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Phe Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Asn Leu Lys Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Met Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys

eolf-seql

145		150		155		160									
Lys	Ser	Ser	Gln	Ser	Val	Leu	Asp	Ser	Ser	Thr	Asn	Lys	Asn	Ser	Leu
			165					170						175	
Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	Lys	Leu	Leu	Leu	Ser
			180					185					190		
Trp	Ala	Ser	Thr	Arg	Glu	Ser	Gly	Ile	Pro	Asp	Arg	Phe	Ser	Gly	Ser
		195					200					205			
Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asp	Ser	Leu	Gln	Pro	Glu
	210					215					220				
Asp	Ser	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Ala	His	Phe	Pro	Ile	Thr
225					230					235					240
Phe	Gly	Gln	Gly	Thr	Arg	Leu	Asp	Ile	Lys	Ser	Gly	Gly	Gly	Gly	Ser
				245				250						255	
Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
			260					265					270		
Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Lys	Tyr
		275				280						285			
Ala	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	290					295					300				
Ala	Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp
305					310					315					320
Ser	Val	Lys	Asp	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr
				325				330						335	
Ala	Tyr	Leu	Gln	Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr
			340					345					350		
Tyr	Cys	Val	Arg	His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Ile	Ser	Tyr	Trp

eolf-seql

355

360

365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 90

<211> 1515

<212> DNA

<213> artificial

<220>

<223> CD33 B3 HL x I2C HL

<400> 90

cagggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggct 60

tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120

eolf-seql

ccaggacagg gtttagagtg gatgggctgg ataaacacct acactggaga gacaaactat	180
gctgataagt tccagggacg cgttaccttc acttcggata cctctaccag cactgcctat	240
atggaactcc gcaacctcaa aagtgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc	360
tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg	420
atgacacagt ctccagactc catgactgtg tctctgggcg agaggaccac catcaactgc	480
aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag	540
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gtcagagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc	840
tctggattca cttcaataa gtacgccatg aactgggtcc gccagggtcc aggaaagggt	900
ttggaatggg ttgctcgcgcat aagaagtaaa tataataatt atgcaacata ttatgccgat	960
tcagtgaaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa	1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc	1080
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tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat	1440
gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtttcgg tggaggaacc	1500
aaactgactg tccta	1515

<210> 91
 <211> 122
 <212> PRT

eolf-seql

<213> artificial

<220>

<223> CD33 VH of F2

<400> 91

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Phe Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Asn Leu Lys Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 92

<211> 5

<212> PRT

<213> artificial

<220>

<223> CD33 HCDR1 of F2

<400> 92

Asn Tyr Gly Met Asn
1 5

eolf-seql

<210> 93
 <211> 17
 <212> PRT
 <213> artificial

<220>
 <223> CD33 HCDR2 of F2

<400> 93

Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Thr	Asn	Tyr	Ala	Asp	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 94
 <211> 13
 <212> PRT
 <213> artificial

<220>
 <223> CD33 HCDR3 of F2

<400> 94

Trp	Ser	Trp	Ser	Asp	Gly	Tyr	Tyr	Val	Tyr	Phe	Asp	Tyr
1				5					10			

<210> 95
 <211> 366
 <212> DNA
 <213> artificial

<220>
 <223> CD33 VH of F2

<400> 95

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tcctgcaagg	ctagcgggta	taccttcaca	aactatggaa	tgaactgggt	gaagcaggct	120
ccaggacagg	gtttagagt	gatgggctgg	ataaacacct	acactggaga	gacaaactat	180
gctgataagt	tccagggacg	cgttaccttc	acttcggata	cctctaccag	cactgcctat	240
atggaactcc	gcaacctcaa	aagtgatgac	acggctgtat	attactgtgc	gcgctggagt	300

eolf-seql

tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360

tcctca 366

<210> 96

<211> 113

<212> PRT

<213> artificial

<220>

<223> CD33 VL of F2

<400> 96

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ser Val Ser Leu Gly
1 5 10 15

Glu Arg Thr Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser
20 25 30

Ser Thr Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Asp Ser Leu Gln Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln
85 90 95

Ser Ala His Phe Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile
100 105 110

Lys

<210> 97

<211> 17

<212> PRT

<213> artificial

eolf-seql

<220>

<223> CD33 LCDR1 of F2

<400> 97

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
1 5 10 15

Ala

<210> 98

<211> 7

<212> PRT

<213> artificial

<220>

<223> CD33 LCDR2 of F2

<400> 98

Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 99

<211> 9

<212> PRT

<213> artificial

<220>

<223> CD33 LCDR3 of F2

<400> 99

Gln Gln Ser Ala His Phe Pro Ile Thr
1 5

<210> 100

<211> 339

<212> DNA

<213> artificial

<220>

<223> CD33 VL of F2

<400> 100

gacatcgtga tgacacagtc tccagactcc ctgtctgtgt ctctgggcga gaggaccacc 60

eolf-seql

atcaactgca agtccagcca gagtgtttta gacagctcca cgaataagaa ctccttagct 120
 tgggtaccagc agaaaccagg acagcctcct aaattactcc tttcctgggc atctacgcgg 180
 gaatccggga tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcact 240
 attgacagcc tgcagcctga agattctgca acttactatt gtcaacagtc tgcccacttc 300
 ccgatcacct ttggccaagg gacacgactg gagattaaa 339

<210> 101
 <211> 250
 <212> PRT
 <213> artificial

<220>
 <223> CD33 HL of F2

<400> 101

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe
 50 55 60

Gln Gly Arg Val Thr Phe Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Asn Leu Lys Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125

eolf-seql

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Ser Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
245 250

<210> 102

<211> 750

<212> DNA

<213> artificial

<220>

<223> CD33 HL of F2

<400> 102

caggtgcagc tggatgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggtc 60

tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120

ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gacaaactat 180

gctgataagt tccaggagcg cgttaccttc acttcggata cctctaccag cactgcctat 240

atggaactcc gcaacctcaa aagtgatgac acggctgtat attactgtgc gcgctggagt 300

eolf-seql

tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
 tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg 420
 atgacacagt ctccagactc cctgtctgtg tctctgggcg agaggaccac catcaactgc 480
 aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag 540
 cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
 atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc 660
 ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
 tttggccaag ggacacgact ggagattaaa 750

<210> 103
 <211> 505
 <212> PRT
 <213> artificial

<220>
 <223> CD33 F2 HL x H2C HL

<400> 103

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe
 50 55 60

Gln Gly Arg Val Thr Phe Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Asn Leu Lys Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp

eolf-seql

100

105

110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Ser Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp

eolf-seql																		
305						310						315						320
Ser	Val	Lys	Asp	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr			
				325					330					335				
Ala	Tyr	Leu	Gln	Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr			
			340					345					350					
Tyr	Cys	Val	Arg	His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Ile	Ser	Tyr	Trp			
		355					360					365						
Ala	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly			
	370					375					380							
Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Thr	Val	Val			
385					390					395					400			
Thr	Gln	Glu	Pro	Ser	Leu	Thr	Val	Ser	Pro	Gly	Gly	Thr	Val	Thr	Leu			
				405					410					415				
Thr	Cys	Gly	Ser	Ser	Thr	Gly	Ala	Val	Thr	Ser	Gly	Tyr	Tyr	Pro	Asn			
			420					425					430					
Trp	Val	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Gly	Leu	Ile	Gly	Gly			
		435					440					445						
Thr	Lys	Phe	Leu	Ala	Pro	Gly	Thr	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu			
	450					455					460							
Leu	Gly	Gly	Lys	Ala	Ala	Leu	Thr	Leu	Ser	Gly	Val	Gln	Pro	Glu	Asp			
465					470					475					480			
Glu	Ala	Glu	Tyr	Tyr	Cys	Ala	Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe			
				485					490					495				
Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu										
			500					505										

<210> 104

eolf-seql

<211> 1515
<212> DNA
<213> artificial

<220>
<223> CD33 F2 HL x H2C HL

<400> 104
caggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggct 60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120
ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gacaaactat 180
gctgataagt tccaggagcg cggtaccttc acttcggata cctctaccag cactgcctat 240
atggaactcc gcaacctcaa aagtgatgac acggctgtat attactgtgc gcgctggagt 300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360
tcctcagggtg gtggtgggtc tggcggcggc ggctccgggtg gtggtgggtc tgacatcgtg 420
atgacacagt ctccagactc cctgtctgtg tctctgggcg agaggaccac catcaactgc 480
aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag 540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
atccctgacc gattcagtggt cagcgggtct gggacagatt tcactctcac tattgacagc 660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg 780
gtcagagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc 840
tctggattca cttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt 900
ttggaatggg ttgctcgcat aagaagtaaa tataataatt atgcaacata ttatgccgat 960
tcagtgaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080
ggtaatagct acatataccta ctgggcttac tggggccaag ggactctggt caccgtctcc 1140
tcaggtggtg gtggttcttg cggcggcggc tccgggtggtg gtggttctca gactgttgtg 1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
tcgactgggg ctgttacatc tggctactac ccaaactggg tccaacaaaa accaggtcag 1320

eolf-seql

gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
 tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
 gaggcagaat attactgtgc tctatggtac agcaaccgct ggggtgttcgg tggaggaacc 1500
 aaactgactg tccta 1515

<210> 105
 <211> 505
 <212> PRT
 <213> artificial

<220>
 <223> CD33 F2 HL x F12Q HL

<400> 105

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe
 50 55 60

Gln Gly Arg Val Thr Phe Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Asn Leu Lys Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser

eolf-seql

130

135

140

Pro Asp Ser Leu Ser Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
 165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
 180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
 210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
 225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr

eolf-seql

340

345

350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
 355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
 385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
 405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
 420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
 435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
 450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
 465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
 485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
 500 505

<210> 106

<211> 1515

<212> DNA

<213> artificial

<220>

<223> CD33 F2 HL x F12Q HL

<400> 106

eolf-seql

cagggtgcagc	tggtgcagtc	tgagagctgag	gtgaagaagc	ctggagagtc	agtcaaggtc	60
tcctgcaagg	ctagcgggta	taccttcaca	aactatggaa	tgaactgggt	gaagcaggct	120
ccaggacagg	gttttagagt	gatgggctgg	ataaacacct	acactggaga	gacaaactat	180
gctgataagt	tccagggacg	cgttaccttc	acttcggata	cctctaccag	cactgcctat	240
atggaactcc	gcaacctcaa	aagtgatgac	acggctgtat	attactgtgc	gcgctggagt	300
tgagtgatg	gttactacgt	ttactttgac	tactggggcc	aaggcactac	ggtcaccgtc	360
tcctcaggtg	gtggtggttc	tggcggcggc	ggctccggtg	gtggtggttc	tgacatcgtg	420
atgacacagt	ctccagactc	cctgtctgtg	tctctgggcg	agaggaccac	catcaactgc	480
aagtccagcc	agagtgtttt	agacagctcc	acgaataaga	actccttagc	ttggtaccag	540
cagaaaccag	gacagcctcc	taaattactc	ctttcctggg	catctacgcg	ggaatccggg	600
atccctgacc	gattcagtgg	cagcgggtct	gggacagatt	tcactctcac	tattgacagc	660
ctgcagcctg	aagattctgc	aacttactat	tgtcaacagt	ctgcccactt	cccgatcacc	720
tttggccaag	ggacacgact	ggagattaaa	tccggagggtg	gtggctccga	ggtgcagctg	780
gtcgagtctg	gaggaggatt	ggtgcagcct	ggagggtcat	tgaaactctc	atgtgcagcc	840
tctggattca	ccttcaatag	ctacgccatg	aactgggtcc	gccaggctcc	aggaaagggt	900
ttggaatggg	ttgctcgcag	aagaagtaaa	tataataatt	atgcaacata	ttatgccgat	960
tcagtgaaag	gcaggttcac	catctccaga	gatgattcaa	aaaacactgc	ctatctacaa	1020
atgaacaact	tgaaaactga	ggacactgcc	gtgtactact	gtgtgagaca	tgggaacttc	1080
ggtaatagct	acgtttcctg	gtgggcttac	tggggccaag	ggactctggt	caccgtctcc	1140
tcaggtgggtg	gtggttctgg	cggcggcggc	tccggtgggtg	gtggttctca	gactgttgtg	1200
actcaggaac	cttcactcac	cgtatcacct	ggtggaacag	tcacactcac	ttgtggctcc	1260
tcgactgggg	ctgttacatc	tggcaactac	ccaaactggg	tccaacaaaa	accaggtcag	1320
gcaccccgtg	gtctaataag	tgggactaag	ttcctcgccc	ccggtactcc	tgccagattc	1380
tcaggctccc	tgcttggagg	caaggctgcc	ctcaccctct	caggggtaca	gccagaggat	1440
gaggcagaat	attactgtgt	tctatggtac	agcaaccgct	gggtgttcgg	tggaggaacc	1500
aaactgactg	tccta					1515

eolf-seql

<210> 107
 <211> 505
 <212> PRT
 <213> artificial

<220>
 <223> CD33 F2 HL x I2C HL

<400> 107

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Thr Asn Tyr Ala Asp Lys Phe
 50 55 60

Gln Gly Arg Val Thr Phe Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Arg Asn Leu Lys Ser Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
 130 135 140

Pro Asp Ser Leu Ser Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu

eolf-seql
170

165

175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly

eolf-seql

370

375

380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 108
<211> 1515
<212> DNA
<213> artificial

<220>
<223> CD33 F2 HL x I2C HL

<400> 108
cagggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggct 60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120
ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gacaaactat 180
gctgataagt tccagggacg cgttaccttc acttcggata cctctaccag cactgcctat 240

eolf-seql

atggaactcc gcaacctcaa aagtgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc	360
tcctcaggtg gtggtggttc tggcggcggc ggctccgggtg gtggtggttc tgacatcgtg	420
atgacacagt ctccagactc cctgtctgtg tctctgggcg agaggaccac catcaactgc	480
aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag	540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg	600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc	660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc	720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg	780
gtcagagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc	840
tctggattca cttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt	900
ttggaatggg ttgctcgcat aagaagtaaa tataataatt atgcaacata ttatgccgat	960
tcagtgaaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa	1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc	1080
ggtaatagct acatatccta ctgggcttac tggggccaag ggactctggt caccgtctcc	1140
tcaggtgggtg gtggttctgg cggcggcggc tccgggtgggt gtggttctca gactgttgtg	1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc	1260
tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag	1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc	1380
tcaggctccc tgcttgagg caaggctgcc ctcaccctct caggggtaca gccagaggat	1440
gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtgttcgg tggaggaacc	1500
aaactgactg tccta	1515

<210> 109

<211> 122

<212> PRT

<213> artificial

<220>

<223> CD33 VH of B10

eolf-seql

<400> 109

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Arg Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 110

<211> 5

<212> PRT

<213> artificial

<220>

<223> CD33 HCDR1 of B10

<400> 110

Asn Tyr Gly Met Asn
1 5

<210> 111

<211> 17

<212> PRT

eolf-seql

<213> artificial

<220>

<223> CD33HCDR2 of B10

<400> 111

Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	Ala	Asp	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 112

<211> 13

<212> PRT

<213> artificial

<220>

<223> CD33 HCDR3 of B10

<400> 112

Trp	Ser	Trp	Ser	Asp	Gly	Tyr	Tyr	Val	Tyr	Phe	Asp	Tyr
1				5					10			

<210> 113

<211> 366

<212> DNA

<213> artificial

<220>

<223> CD33 VH of B10

<400> 113

caggtgcagc	tggtgcagtc	tggagctgag	gtgaagaagc	ctggtgagtc	agtcaaggtc	60
tcctgcaagg	ctagcgggta	taccttcaca	aactatggaa	tgaactgggt	gaagcaggct	120
ccaggacagg	gtttagagtg	gatgggctgg	ataaacacct	acactggaga	gccaacctat	180
gctgataagt	tccaggagcg	cgttaccatg	actacggata	cctctaccag	cactgcctat	240
atggaaatcc	gcaacctcag	aagtgatgac	acggctgtat	attactgtgc	gcgctggagt	300
tggagtgatg	gttactacgt	ttactttgac	tactggggcc	aaggcactac	ggtcaccgtc	360
tcctca						366

eolf-seql

<210> 114
 <211> 113
 <212> PRT
 <213> artificial

<220>
 <223> CD33 VL of B10

<400> 114

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Thr Val Ser Leu Gly
 1 5 10 15

Glu Arg Thr Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser
 20 25 30

Ser Asn Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Pro Pro Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile
 50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Asp Gly Leu Gln Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln
 85 90 95

Ser Ala His Phe Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile
 100 105 110

Lys

<210> 115
 <211> 17
 <212> PRT
 <213> artificial

<220>
 <223> CD33 LCDR1 of B10

<400> 115

eolf-seql

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Asn Asn Lys Asn Ser Leu
1 5 10 15

Ala

<210> 116
<211> 7
<212> PRT
<213> artificial

<220>
<223> CD33 LCDR2 of B10

<400> 116

Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 117
<211> 9
<212> PRT
<213> artificial

<220>
<223> CD33 LCDR3 of B10

<400> 117

Gln Gln Ser Ala His Phe Pro Ile Thr
1 5

<210> 118
<211> 339
<212> DNA
<213> artificial

<220>
<223> CD33 VL of B10

<400> 118
gacatcgtga tgacacagtc tccagactcc ctgactgtgt ctctgggcga gaggaccacc 60
atcaactgca agtccagcca gagtgtttta gacagctcca acaataagaa ctccttagct 120
tggtaccagc agaaaccagg acagcctcct aaattactcc tttcctgggc atctacgcgg 180

eolf-seql

gaatccggga tccctgaccg attcagtggc agcggttctg ggacagattt cactctcact 240
attgacggcc tgcagcctga agattctgca acttactatt gtcaacagtc tgcccacttc 300
ccgatcacct ttggccaagg gacacgactg gagattaa 339

<210> 119
<211> 250
<212> PRT
<213> artificial

<220>
<223> CD33 HL of B10

<400> 119

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Arg Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

eolf-seql

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Asn Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Gly Leu Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
245 250

<210> 120

<211> 750

<212> DNA

<213> artificial

<220>

<223> CD33 HL of B10

<400> 120

caggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggtgagtc agtcaaggct 60

tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120

ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gccaacctat 180

gctgataagt tccaggagc cgttaccatg actacggata cctctaccag cactgcctat 240

atggaaatcc gcaacctcag aagtgatgac acggctgtat attactgtgc gcgctggagt 300

tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc 360

tcctcagggtg gtggtgggtc tggcggcggc ggctccggtg gtggtgggtc tgacatcgtg 420

eolf-seql

atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
aagtccagcc agagtgtttt agacagctcc aacaataaga actccttagc ttggtaccag 540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
atccctgacc gattcagtgg cagcggttct gggacagatt tcactctcac tattgacggc 660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
tttggccaag ggacacgact ggagattaaa 750

<210> 121
<211> 505
<212> PRT
<213> artificial

<220>
<223> CD33 B10 HL x H2C HL

<400> 121

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Arg Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly

eolf-seql

115

120

125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
 130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Asn Asn Lys Asn Ser Leu
 165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
 180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Gly Leu Gln Pro Glu
 210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
 225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr

eolf-seql
330

325

335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 122
<211> 1515
<212> DNA
<213> artificial

eolf-seql

<220>

<223> CD33 B10 HL x H2C HL

<400> 122

caggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggtgagtc agtcaaggtc	60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct	120
ccaggacagg gtttagagtg gatgggctgg ataaacacct acactggaga gccaacctat	180
gctgataagt tccaggggacg cgttaccatg actacggata cctctaccag cactgcctat	240
atggaaatcc gcaacctcag aagtgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc	360
tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg	420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc	480
aagtccagcc agagtgtttt agacagctcc aacaataaga actccttagc ttggtaccag	540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg	600
atccctgacc gattcagtggt cagcggttct gggacagatt tcactctcac tattgacggc	660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc	720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg	780
gtcagagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaaactctc atgtgcagcc	840
tctggattca cttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt	900
ttggaatggg ttgctcgcgcat aagaagtaaa tataataatt atgcaacata ttatgccgat	960
tcagtgaaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa	1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc	1080
ggtaatagct acatatccta ctgggcttac tggggccaag ggactctggt caccgtctcc	1140
tcaggtggtg gtggttcttg cggcggcggc tccggtggtg gtggttctca gactgttggtg	1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc	1260
tcgactgggg ctgttacatc tggctactac ccaaactggg tccaacaaaa accaggtcag	1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc	1380
tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat	1440

eolf-seql

gaggcagaat attactgtgc tctatggtag agcaaccgct ggggtgttcgg tggaggaacc 1500

aaactgactg tccta 1515

<210> 123

<211> 505

<212> PRT

<213> artificial

<220>

<223> CD33 B10 HL x F12Q HL

<400> 123

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Arg Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys

eolf-seql

145		150		155		160									
Lys	Ser	Ser	Gln	Ser	Val	Leu	Asp	Ser	Ser	Asn	Asn	Lys	Asn	Ser	Leu
			165						170					175	
Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	Lys	Leu	Leu	Leu	Ser
			180					185					190		
Trp	Ala	Ser	Thr	Arg	Glu	Ser	Gly	Ile	Pro	Asp	Arg	Phe	Ser	Gly	Ser
		195					200					205			
Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asp	Gly	Leu	Gln	Pro	Glu
	210					215					220				
Asp	Ser	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Ala	His	Phe	Pro	Ile	Thr
225					230					235					240
Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys	Ser	Gly	Gly	Gly	Gly	Ser
				245					250					255	
Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
			260					265					270		
Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Ser	Tyr
		275				280						285			
Ala	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	290					295					300				
Ala	Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp
305					310					315					320
Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr
				325					330					335	
Ala	Tyr	Leu	Gln	Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr
			340					345					350		
Tyr	Cys	Val	Arg	His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Val	Ser	Trp	Trp

eolf-seql

355

360

365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 124
<211> 1515
<212> DNA
<213> artificial

<220>
<223> CD33 B10 HL x F12Q HL

<400> 124
cagggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggtgagtc agtcaaggct 60

tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120

eolf-seql

ccaggacagg gtttagagt gatgggctgg ataaacacct acactggaga gccaacctat	180
gctgataagt tccagggacg cgttaccatg actacggata cctctaccag cactgcctat	240
atggaaatcc gcaacctcag aagtgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc	360
tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg	420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc	480
aagtccagcc agagtgtttt agacagctcc aacaataaga actccttagc ttggtaccag	540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg	600
atccctgacc gattcagtgg cagcggttct gggacagatt tcactctcac tattgacggc	660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc	720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg	780
gtcagagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc	840
tctggattca ccttcaatag ctacgccatg aactgggtcc gccagggtcc aggaaagggt	900
ttggaatggg ttgctcgc atagaagtaaa tataataatt atgcaacata ttatgccgat	960
tcagtgaaag gcaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa	1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc	1080
ggtaatagct acgtttcctg gtgggcttac tggggccaag ggactctggt caccgtctcc	1140
tcagggtggtg gtggttctgg cggcggcggc tccgggtggtg gtggttctca gactgttggtg	1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc	1260
tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag	1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc	1380
tcaggctccc tgcttgagg caaggctgcc ctcaccctct caggggtaca gccagaggat	1440
gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtttcgg tggaggaacc	1500
aaactgactg tccta	1515

<210> 125
 <211> 505
 <212> PRT

eolf-seql

<213> artificial

<220>

<223> CD33 B10 HL x I2C HL

<400> 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Arg Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Asn Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser

eolf-seql

180

185

190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Gly Leu Gln Pro Glu
 210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
 225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
 355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val

eolf-seql

385	390	395	400
Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu	405	410	415
Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn	420	425	430
Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly	435	440	445
Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu	450	455	460
Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp	465	470	475
Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe	485	490	495
Gly Gly Gly Thr Lys Leu Thr Val Leu	500	505	

<210> 126
 <211> 1515
 <212> DNA
 <213> artificial

<220>
 <223> CD33 B10 HL x I2C HL

<400> 126	
caggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggtgagtc agtcaaggct	60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct	120
ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gccaacctat	180
gctgataagt tccaggagcg cgttaccatg actacggata cctctaccag cactgcctat	240
atggaaatcc gcaacctcag aagtgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcactac ggtcaccgtc	360

eolf-seql

tcctcaggtg gtggtggttc tggcggcggc ggctccgggtg gtggtggttc tgacatcgtg	420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc	480
aagtccagcc agagtgtttt agacagctcc aacaataaga actccttagc ttggtaccag	540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg	600
atccctgacc gattcagtgg cagcggttct gggacagatt tcactctcac tattgacggc	660
ctgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc	720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg	780
gtcagagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc	840
tctggattca ctttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt	900
ttggaatggg ttgctcgcac aagaagtaaa tataataatt atgcaacata ttatgccgat	960
tcagtgaaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa	1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc	1080
ggtaatagct acatatccta ctgggcttac tggggccaag ggactctggt caccgtctcc	1140
tcagggtggtg gtggttcttg cggcggcggc tccgggtggtg gtggttctca gactgttggtg	1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc	1260
tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag	1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc	1380
tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat	1440
gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtgttcgg tggaggaacc	1500
aaactgactg tccta	1515

<210> 127
 <211> 122
 <212> PRT
 <213> artificial

<220>
 <223> CD33 VH of E11

<400> 127

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu

eolf-seql

1	5	10	15
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
 50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Ile Arg Asn Leu Gly Gly Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser
 115 120

<210> 128
 <211> 5
 <212> PRT
 <213> artificial

<220>
 <223> CD33 HCDR1 of E11

<400> 128

Asn Tyr Gly Met Asn
 1 5

<210> 129
 <211> 17
 <212> PRT
 <213> artificial

<220>
 <223> CD33 HCDR2 of E11

eolf-seql

<400> 129

Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	Ala	Asp	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 130

<211> 13

<212> PRT

<213> artificial

<220>

<223> CD33 HCDR3 of E11

<400> 130

Trp	Ser	Trp	Ser	Asp	Gly	Tyr	Tyr	Val	Tyr	Phe	Asp	Tyr
1				5					10			

<210> 131

<211> 366

<212> DNA

<213> artificial

<220>

<223> CD33 VH of E11

<400> 131

cagggtgcagc	tggtgcagtc	tggagctgag	gtgaagaagc	ctggagagtc	agtcaaggctc	60
tcctgcaagg	ctagcgggta	taccttcaca	aactatggaa	tgaactgggt	gaagcaggct	120
ccaggacagg	gtttagagtg	gatgggctgg	ataaacacct	acactggaga	gccaacctat	180
gctgataagt	tccagggacg	cgttaccatg	actacggata	cctctaccag	cactgcctat	240
atggaaatcc	gcaacctcgg	aggtgatgac	acggctgtat	attactgtgc	gcgctggagt	300
tggagtgatg	gttactacgt	ttactttgac	tactggggcc	aaggcacttc	ggtcaccgtc	360
tcctca						366

<210> 132

<211> 113

<212> PRT

eolf-seql

<213> artificial

<220>

<223> CD33 VL of E11

<400> 132

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Thr Val Ser Leu Gly
1 5 10 15

Glu Arg Thr Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser
20 25 30

Ser Thr Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Asp Ser Pro Gln Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln
85 90 95

Ser Ala His Phe Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile
100 105 110

Lys

<210> 133

<211> 17

<212> PRT

<213> artificial

<220>

<223> CD33 LCDR1 of E11

<400> 133

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
1 5 10 15

eolf-seql

Ala

<210> 134
 <211> 7
 <212> PRT
 <213> artificial

<220>
 <223> CD33 LCDR2 of E11

<400> 134

Trp Ala Ser Thr Arg Glu Ser
 1 5

<210> 135
 <211> 9
 <212> PRT
 <213> artificial

<220>
 <223> CD33 LCDR3 of E11

<400> 135

Gln Gln Ser Ala His Phe Pro Ile Thr
 1 5

<210> 136
 <211> 339
 <212> DNA
 <213> artificial

<220>
 <223> CD33 VL of E11

<400> 136
 gacatcgtga tgacacagtc tccagactcc ctgactgtgt ctctgggcga gaggaccacc 60
 atcaactgca agtccagcca gagtgtttta gacagctcca cgaataagaa ctccttagct 120
 tggtaccagc agaaaccagg acagcctcct aaattactcc tttcctgggc atctacgcgg 180
 gaatccggga tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcact 240
 attgacagcc cgcagcctga agattctgca acttactatt gtcaacagtc tgcccacttc 300

ccgatcacct ttggccaagg gacacgactg gagattaaa

339

<210> 137

<211> 250

<212> PRT

<213> artificial

<220>

<223> CD33 HL of E11

<400> 137

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
 50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Ile Arg Asn Leu Gly Gly Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
 130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

eolf-seql

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Pro Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
245 250

<210> 138
<211> 750
<212> DNA
<213> artificial

<220>
<223> CD33 HL of E11

<400> 138
cagggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggct 60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120
ccaggacagg gtttagagtg gatgggctgg ataaacacct acactggaga gccaacctat 180
gctgataagt tccagggacg cgttaccatg actacggata cctctaccag cactgcctat 240
atggaaatcc gcaacctcgg aggtgatgac acggctgtat attactgtgc gcgctggagt 300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcacttc ggtcaccgtc 360
tcctcaggtg gtggtggttc tggcggcggc ggctccggtg gtggtggttc tgacatcgtg 420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag 540

eolf-seql

cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc 660
ccgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
tttggccaag ggacacgact ggagattaata 750

<210> 139
<211> 505
<212> PRT
<213> artificial

<220>
<223> CD33 E11 HL x H2C HL

<400> 139

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Arg Asn Leu Gly Gly Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser

eolf-seql

130

135

140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
 165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
 180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Pro Gln Pro Glu
 210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
 225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr

eolf-seql

340

345

350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 140

<211> 1515

<212> DNA

<213> artificial

<220>

<223> CD33 E11 HL x H2C HL

<400> 140

eolf-seql

cagggtgcagc	tggtgcagtc	tgagagctgag	gtgaagaagc	ctggagagtc	agtcaaggtc	60
tcctgcaagg	ctagcgggta	taccttcaca	aactatggaa	tgaactgggt	gaagcaggct	120
ccaggacagg	gttttagagt	gatgggctgg	ataaacacct	acactggaga	gccaacctat	180
gctgataagt	tccagggacg	cgttaccatg	actacggata	cctctaccag	cactgcctat	240
atggaaatcc	gcaacctcgg	aggtgatgac	acggctgtat	attactgtgc	gcgctggagt	300
tgagtgatg	gttactacgt	ttactttgac	tactggggcc	aaggcacttc	ggtcaccgtc	360
tcctcaggtg	gtggtggttc	tggcggcggc	ggctccggtg	gtggtggttc	tgacatcgtg	420
atgacacagt	ctccagactc	cctgactgtg	tctctgggcg	agaggaccac	catcaactgc	480
aagtccagcc	agagtgtttt	agacagctcc	acgaataaga	actccttagc	ttggtaccag	540
cagaaaccag	gacagcctcc	taaattactc	ctttcctggg	catctacgcg	ggaatccggg	600
atccctgacc	gattcagtgg	cagcgggtct	gggacagatt	tcactctcac	tattgacagc	660
ccgcagcctg	aagattctgc	aacttactat	tgtcaacagt	ctgcccactt	cccgatcacc	720
tttggccaag	ggacacgact	ggagattaaa	tccggagggtg	gtggctccga	ggtgcagctg	780
gtcgagtctg	gaggaggatt	ggtgcagcct	ggagggtcat	tgaaactctc	atgtgcagcc	840
tctggattca	ccttcaataa	gtacgccatg	aactgggtcc	gccaggctcc	aggaaagggt	900
ttggaatggg	ttgctcgcag	aagaagtaaa	tataataatt	atgcaacata	ttatgccgat	960
tcagtgaaag	acaggttcac	catctccaga	gatgattcaa	aaaacactgc	ctatctacaa	1020
atgaacaact	tgaaaactga	ggacactgcc	gtgtactact	gtgtgagaca	tgggaacttc	1080
ggtaatagct	acatatccta	ctgggcttac	tggggccaag	ggactctggt	caccgtctcc	1140
tcaggtgggtg	gtggttctgg	cggcggcggc	tccggtgggtg	gtggttctca	gactgttgtg	1200
actcaggaac	cttcactcac	cgtatcacct	ggtggaacag	tcacactcac	ttgtggctcc	1260
tcgactgggg	ctgttacatc	tggctactac	ccaaactggg	tccaacaaaa	accaggtcag	1320
gcaccccgtg	gtctaataag	tgggactaag	ttcctcgccc	ccggtactcc	tgccagattc	1380
tcaggctccc	tgcttggagg	caaggctgcc	ctcaccctct	caggggtaca	gccagaggat	1440
gaggcagaat	attactgtgc	tctatggtac	agcaaccgct	gggtgttcgg	tggaggaacc	1500
aaactgactg	tccta					1515

eolf-seql

<210> 141
 <211> 505
 <212> PRT
 <213> artificial

<220>
 <223> CD33 E11 HL x F12Q HL

<400> 141

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
 50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

Met Glu Ile Arg Asn Leu Gly Gly Asp Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
 100 105 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
 130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
 145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu

eolf-seql
170

165

175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Pro Gln Pro Glu
210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
305 310 315 320

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly

eolf-seql

370

375

380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
405 410 415

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
420 425 430

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
435 440 445

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
450 455 460

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
465 470 475 480

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
485 490 495

Gly Gly Gly Thr Lys Leu Thr Val Leu
500 505

<210> 142
<211> 1515
<212> DNA
<213> artificial

<220>
<223> CD33 E11 HL x F12Q HL

<400> 142
cagggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggct 60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120
ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gccaacctat 180
gctgataagt tccagggacg cgttaccatg actacggata cctctaccag cactgcctat 240

eolf-seql

atggaaatcc gcaacctcgg aggtgatgac acggctgtat attactgtgc gcgctggagt	300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcacttc ggtcaccgtc	360
tcctcaggtg gtggtggttc tggcggcggc ggctccgggtg gtggtggttc tgacatcgtg	420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc	480
aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag	540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg	600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc	660
ccgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc	720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg	780
gtcagagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc	840
tctggattca cttcaatag ctacgccatg aactgggtcc gccaggctcc aggaaagggt	900
ttggaatggg ttgctcgcat aagaagtaaa tataataatt atgcaacata ttatgccgat	960
tcagtgaaag gcaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa	1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc	1080
ggtaatagct acgtttcctg gtgggcttac tggggccaag ggactctggt caccgtctcc	1140
tcaggtggtg gtggttctgg cggcggcggc tccgggtggtg gtggttctca gactgttgtg	1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc	1260
tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag	1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc	1380
tcaggctccc tgcttgagg caaggctgcc ctcaccctct caggggtaca gccagaggat	1440
gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtgttcgg tggaggaacc	1500
aaactgactg tccta	1515

<210> 143

<211> 505

<212> PRT

<213> artificial

<220>

<223> CD33 E11 HL x I2C HL

eolf-seql

<400> 143

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Ile Arg Asn Leu Gly Gly Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser
130 135 140

Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys
145 150 155 160

Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser
180 185 190

Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser

eolf-seql

195

200

205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Pro Gln Pro Glu
 210 215 220

Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr
 225 230 235 240

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser
 245 250 255

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 260 265 270

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 275 280 285

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 290 295 300

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 305 310 315 320

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 325 330 335

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 340 345 350

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
 355 360 365

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 370 375 380

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
 385 390 395 400

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu

eolf-seql															
405								410				415			
Thr	Cys	Gly	Ser	Ser	Thr	Gly	Ala	Val	Thr	Ser	Gly	Asn	Tyr	Pro	Asn
			420				425						430		
Trp	Val	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Gly	Leu	Ile	Gly	Gly
			435				440						445		
Thr	Lys	Phe	Leu	Ala	Pro	Gly	Thr	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Leu
			450				455						460		
Leu	Gly	Gly	Lys	Ala	Ala	Leu	Thr	Leu	Ser	Gly	Val	Gln	Pro	Glu	Asp
465			470						475			480			
Glu	Ala	Glu	Tyr	Tyr	Cys	Val	Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val	Phe
			485						490			495			
Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu							
			500			505									

eolf-seql

aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag	540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg	600
atccctgacc gattcagtgg cagcgggtct gggacagatt tcactctcac tattgacagc	660
ccgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc	720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg	780
gtcgagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc	840
tctggattca ctttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt	900
ttggaatggg ttgctcgcac aagaagtaaa tataataatt atgcaacata ttatgccgat	960
tcagtgaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa	1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc	1080
ggtaatagct acatatccta ctgggcttac tggggccaag ggactctggt caccgtctcc	1140
tcagggtggtg gtggttctgg cggcggcggc tccgggtggtg gtggttctca gactgttgtg	1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc	1260
tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag	1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc	1380
tcaggctccc tgcttgagg caaggctgcc ctcaccctct caggggtaca gccagaggat	1440
gaggcagaat attactgtgt tctatggtac agcaaccgct gggtgttcgg tggaggaacc	1500
aaactgactg tccta	1515

<210> 145
 <211> 1125
 <212> DNA
 <213> human

<400> 145	
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ccaaatttct ggctgcaagt gcaggagtca gtgacggtagc aggagggttt gtgcgtcctc	120
gtgccctgca ctttcttcca tcccataccc tactacgaca agaactcccc agttcatggt	180
tactggttcc gggaaggagc cattatatcc ggggactctc cagtggccac aaacaagcta	240
gatcaagaag tacaggagga gactcagggc agattccgcc tccttgggga tcccagtagg	300

eolf-seql

aacaactgct ccctgagcat cgtagacgcc aggaggaggg ataatggttc atacttcttt 360
 cggatggaga gaggaagtac caaatacagt tacaaatctc cccagctctc tgtgcatgtg 420
 acagacttga cccacaggcc caaaatcctc atccctggca ctctagaacc cggccactcc 480
 aaaaacctga cctgctctgt gtcctgggcc tgtgagcagg gaacaccccc gatcttctcc 540
 tggttgtcag ctgccccac ctccctgggc cccaggacta ctactcctc ggtgctcata 600
 atcacccac ggccccagga ccacggcacc aacctgacct gtcaggtgaa gttcgctgga 660
 gctggtgtga ctacggagag aaccatccag ctcaacgtca cctatgttcc acagaacca 720
 acaactggta tctttccagg agatggctca gggaaacaag agaccagagc aggagtggtt 780
 catggggcca ttggaggagc tgggtgttaca gccctgctcg ctctttgtct ctgcctcatc 840
 ttcttcatag tgaagacca caggaggaaa gcagccagga cagcagtggg caggaatgac 900
 acccacccta ccacagggtc agcctccccg aaacaccaga agaagtccaa gttacatggc 960
 cccactgaaa cctcaagctg ttcagggtgcc gccctactg tggagatgga tgaggagctg 1020
 cattatgctt ccctcaactt tcatgggatg aatccttcca aggacacctc caccgaatac 1080
 tcagagggtca ggacccagtc cgggcatcat caccatcatc attga 1125

<210> 146
 <211> 374
 <212> PRT
 <213> human

<400> 146

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
 1 5 10 15

Val His Ser Asp Pro Asn Phe Trp Leu Gln Val Gln Glu Ser Val Thr
 20 25 30

Val Gln Glu Gly Leu Cys Val Leu Val Pro Cys Thr Phe Phe His Pro
 35 40 45

Ile Pro Tyr Tyr Asp Lys Asn Ser Pro Val His Gly Tyr Trp Phe Arg
 50 55 60

eolf-seql

Glu Gly Ala Ile Ile Ser Gly Asp Ser Pro Val Ala Thr Asn Lys Leu
65 70 75 80

Asp Gln Glu Val Gln Glu Glu Thr Gln Gly Arg Phe Arg Leu Leu Gly
85 90 95

Asp Pro Ser Arg Asn Asn Cys Ser Leu Ser Ile Val Asp Ala Arg Arg
100 105 110

Arg Asp Asn Gly Ser Tyr Phe Phe Arg Met Glu Arg Gly Ser Thr Lys
115 120 125

Tyr Ser Tyr Lys Ser Pro Gln Leu Ser Val His Val Thr Asp Leu Thr
130 135 140

His Arg Pro Lys Ile Leu Ile Pro Gly Thr Leu Glu Pro Gly His Ser
145 150 155 160

Lys Asn Leu Thr Cys Ser Val Ser Trp Ala Cys Glu Gln Gly Thr Pro
165 170 175

Pro Ile Phe Ser Trp Leu Ser Ala Ala Pro Thr Ser Leu Gly Pro Arg
180 185 190

Thr Thr His Ser Ser Val Leu Ile Ile Thr Pro Arg Pro Gln Asp His
195 200 205

Gly Thr Asn Leu Thr Cys Gln Val Lys Phe Ala Gly Ala Gly Val Thr
210 215 220

Thr Glu Arg Thr Ile Gln Leu Asn Val Thr Tyr Val Pro Gln Asn Pro
225 230 235 240

Thr Thr Gly Ile Phe Pro Gly Asp Gly Ser Gly Lys Gln Glu Thr Arg
245 250 255

Ala Gly Val Val His Gly Ala Ile Gly Gly Ala Gly Val Thr Ala Leu
260 265 270

eolf-seql

Leu Ala Leu Cys Leu Cys Leu Ile Phe Phe Ile Val Lys Thr His Arg
275 280 285

Arg Lys Ala Ala Arg Thr Ala Val Gly Arg Asn Asp Thr His Pro Thr
290 295 300

Thr Gly Ser Ala Ser Pro Lys His Gln Lys Lys Ser Lys Leu His Gly
305 310 315 320

Pro Thr Glu Thr Ser Ser Cys Ser Gly Ala Ala Pro Thr Val Glu Met
325 330 335

Asp Glu Glu Leu His Tyr Ala Ser Leu Asn Phe His Gly Met Asn Pro
340 345 350

Ser Lys Asp Thr Ser Thr Glu Tyr Ser Glu Val Arg Thr Gln Ser Gly
355 360 365

His His His His His His
370

<210> 147
<211> 1083
<212> DNA
<213> macaque

<400> 147
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gtcaggctgg aagtgcagga gtcagtgaac gtacaggagg gtttgtgcgt ctttgtgccc 120
tgcactttct tccatcccgt accctaccac accaggaatt ccccagttca tggttactgg 180
ttccgggaag gagccattgt atccttggac tctccagtgg ccacaaacaa gctagatcaa 240
gaagtacagg aggagacca gggccgattc cgcctccttg gggatcccag taggaacaac 300
tgctccctga gcatcgtaga tgccaggagg agggataacg gttcatactt ctttcgggatg 360
gagaaaggaa gtaccaaata cagttacaaa tctaccacgc tctctgtgca tgtgacagac 420
ttgaccaca ggccccaaat cctcatccct ggagccctag accctgacca ctccaaaaac 480
ctgacctgct ctgtgccctg ggccctgtgag cagggaacac ctccaatctt ctcttgatg 540

eolf-seql

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tcagctgccc ccacctccct gggcctcagg accactcact cctcggtgct cataatcacc      600
ccacggcccc aggaccacgg caccaacctc acctgtcagg tgaagttccc tggagctggc      660
gtgaccacgg agagaaccat ccagctcaat gtctcctatg cttcacagaa cccaagaact      720
gatatctttc taggagacgg ctcagggaaa caaggagtgg ttcagggagc catcggggga      780
gctggtgtca cagtcttgct cgctctttgt ctctgcctca tcttcttcac agtgaagact      840
cacaggagga aagcagccag gacagcagtg ggcaggatcg acaccaccc cgccacaggg      900
ccaacatcct cgaaacacca gaagaagtcc aagttacatg gcgccactga aacctcaggc      960
tgttcaggta ccacccttac tgtggagatg gatgaggagc tgcactacgc ttccctcaac     1020
tttcatggga tgaatccttc tgaggacacc tccaccgaat actcagaggt caggaccag      1080
tga                                                                    1083

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<210> 148
 <211> 505
 <212> PRT
 <213> artificial

<220>
 <223> CD33 UD H2C HL x AF5 HL

<400> 148

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 65 70 75 80

eolf-seql

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu Ser Gly Gly Gly Gly Ser Gln
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly
275 280 285

eolf-seql

Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met Gly
290 295 300

Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe Lys
305 310 315 320

Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr Leu
325 330 335

Glu Leu His Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp Gly
355 360 365

Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser Pro
385 390 395 400

Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys Lys
405 410 415

Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu Ala
420 425 430

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser Trp
435 440 445

Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly
450 455 460

Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu Asp
465 470 475 480

Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr Phe
485 490 495

eolf-seql

Gly Gln Gly Thr Arg Leu Glu Ile Lys
500 505

<210> 149
<211> 1515
<212> DNA
<213> artificial

<220>
<223> CD33 UD H2C HL x AF5 HL

<400> 149
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tcatgtgcag cctctggatt caccttcaat aagtacgcca tgaactgggt ccgccaggct 120
ccaggaaagg gtttggaatg ggttgctcgc ataagaagta aatataataa ttatgcaaca 180
tattatgccg attcagtga agacagggtc accatctcca gagatgattc aaaaaacact 240
gcctatctac aaatgaacaa cttgaaaact gaggacactg ccgtgtacta ctgtgtgaga 300
catgggaact tcggtaatag ctacatatcc tactgggctt actggggcca agggactctg 360
gtcaccgtct cctcagggtg tgggtggttct ggccggcgcg gctccgggtg tgggtggttct 420
cagactgttg tgactcagga accttcactc accgtatcac ctgggtggaac agtcacactc 480
acttgtggct cctcgactgg ggctgttaca tctggctact acccaaactg ggtccaacaa 540
aaaccagggtc aggcaccccg tggcttaata ggtgggacta agttcctcgc ccccggtact 600
cctgccagat tctcaggctc cctgcttgga ggcaaggctg ccctcacctc ctcaggggta 660
cagccagagg atgaggcaga atattactgt gctctatggg acagcaaccg ctgggtgttc 720
gggtggaggaa ccaaactgac tgtcctatcc ggagggtggg gctcccagggt gcagctgggtc 780
cagtctggag ctgagggtgaa gaagcctgga gcgtcagtca aggtctcctg caaggctagc 840
gggtatacct tcacaaacta tggaatgaac tgggtgaagc aggtccagg acagggttta 900
aagtggatgg gctggataaa cacctacact ggagagccaa catatgctga tgacttcaag 960
ggacgggtta ccatgacttc ggatacctct accagcactg cctatttgga actccacaac 1020
ctcagaagtg atgacacggc tgtatattac tgtgcgcgct ggagttggag tgatgggttac 1080
tacgtttact ttgactactg gggccaaggc actacgggtc ccgtctcctc aggtgggtgg 1140
ggttctggcg gcggcggtc cggtgggtgg ggttctgaca tcgtgatgac acagtctcca 1200

eolf-seql

gactccctga ctgtgtctct gggcgagagg accaccatca actgcaagtc cagccagagt 1260
 gtttttagaca gctccaagaa taagaactcc ttagcttggt accagcagaa accaggacag 1320
 cctcctaaat tactcctttc ctgggcatct acgcgggaat ccgggatccc tgaccgattc 1380
 agtggcagcg ggtctgggac agatttcact ctactattg acagcctgca gcctgaagat 1440
 tctgcaactt actattgtca acagtctgcc cacttcccga tcacctttgg ccaagggaca 1500
 cgactggaga ttaaa 1515

<210> 150
 <211> 505
 <212> PRT
 <213> artificial

<220>
 <223> CD33 UD F12Q HL x AF5 HL

<400> 150

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
 20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
 100 105 110

eolf-seql

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu Ser Gly Gly Gly Gly Ser Gln
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly
275 280 285

Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met Gly
290 295 300

Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe Lys
305 310 315 320

eolf-seq1

Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr Leu
325 330 335

Glu Leu His Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp Gly
355 360 365

Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser Pro
385 390 395 400

Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys Lys
405 410 415

Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu Ala
420 425 430

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser Trp
435 440 445

Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly
450 455 460

Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu Asp
465 470 475 480

Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr Phe
485 490 495

Gly Gln Gly Thr Arg Leu Glu Ile Lys
500 505

<210> 151
<211> 1515
<212> DNA
<213> artificial

eolf-seql

<220>

<223> CD33 UD F12Q HL x AF5 HL

<400> 151

gaggtgcagc tggtcgagtc tggaggagga ttggtgcagc ctggagggtc attgaaactc	60
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ccaggaaagg gtttggaatg gggtgctcgc ataagaagta aatataataa ttatgcaaca	180
tattatgccg attcagtgaaggaggaggttc accatctcca gagatgattc aaaaaacact	240
gcctatctac aaatgaacaa cttgaaaact gaggacactg ccgtgtacta ctgtgtgaga	300
catgggaact tcggtaatag ctacgtttcc tgggtgggctt actggggcca agggactctg	360
gtcaccgtct cctcagggtg tgggtggttct ggcggcggcg gctccgggtg tgggtggttct	420
cagactgttg tgactcagga accttcactc accgtatcac ctggtggaac agtcacactc	480
acttgtggct cctcgactgg ggctgttaca tctggcaact acccaaactg ggtccaacaa	540
aaaccaggtc aggcaccccg tggcttaata ggtgggacta agttcctcgc ccccggtact	600
cctgccagat tctcaggctc cctgcttgga ggcaaggctg ccctcacctc ctcaggggta	660
cagccagagg atgaggcaga atattactgt gttctatgggt acagcaaccg ctgggtgttc	720
gggtggaggaa ccaaactgac tgtcctatcc ggagggtggt gctcccagggt gcagctggtc	780
cagtctggag ctgagggtgaa gaagcctgga gcgtcagtca aggtctcctg caaggctagc	840
gggtatacct tcacaaacta tggaatgaac tgggtgaagc aggtccagg acagggttta	900
aagtggatgg gctggataaa cacctacact ggagagccaa catatgctga tgacttcaag	960
ggacgggtta ccatgacttc ggatacctct accagcactg cctatttgga actccacaac	1020
ctcagaagtg atgacacggc tgtatattac tgtgcgcgct ggagttggag tgatggttac	1080
tacgtttact ttgactactg gggccaaggc actacgggtca ccgtctcctc aggtggtggt	1140
ggttctggcg gcggcggctc cgggtggtggg ggttctgaca tcgtgatgac acagtctcca	1200
gactccctga ctgtgtctct gggcgagagg accaccatca actgcaagtc cagccagagt	1260
gttttagaca gctccaagaa taagaactcc ttagcttggt accagcagaa accaggacag	1320
cctcctaaat tactcctttc ctgggcatct acgcgggaat ccgggatccc tgaccgattc	1380
agtggcagcg ggtctgggac agatttcact ctactattg acagcctgca gcctgaagat	1440

eolf-seql

tctgcaactt actattgtca acagtctgcc cacttcccga tcacctttgg ccaagggaca 1500
cgactggaga ttaaa 1515

<210> 152
<211> 505
<212> PRT
<213> artificial

<220>
<223> CD33 UD I2C HL x AF5 HL

<400> 152

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

eolf-seql

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu Ser Gly Gly Gly Gly Ser Gln
245 250 255

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
260 265 270

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly
275 280 285

Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Lys Trp Met Gly
290 295 300

Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe Lys
305 310 315 320

Gly Arg Val Thr Met Thr Ser Asp Thr Ser Thr Ser Thr Ala Tyr Leu
325 330 335

Glu Leu His Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala
340 345 350

eolf-seql

Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp Gly
355 360 365

Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
370 375 380

Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser Pro
385 390 395 400

Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys Lys
405 410 415

Ser Ser Gln Ser Val Leu Asp Ser Ser Lys Asn Lys Asn Ser Leu Ala
420 425 430

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser Trp
435 440 445

Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly
450 455 460

Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Leu Gln Pro Glu Asp
465 470 475 480

Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr Phe
485 490 495

Gly Gln Gly Thr Arg Leu Glu Ile Lys
500 505

<210> 153
<211> 1515
<212> DNA
<213> artificial

<220>
<223> CD33 UD I2C HL x AF5 HL

<400> 153
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tcatgtgcag cctctggatt caccttcaat aagtacgcca tgaactgggt ccgccaggct 120

eolf-seql

ccaggaaagg gtttggaatg ggttgctcgc ataagaagta aatataataa ttatgcaaca	180
tattatgccg attcagtgaag agacagggttc accatctcca gagatgattc aaaaaacact	240
gcctatctac aaatgaacaa cttgaaaact gaggacactg ccgtgtacta ctgtgtgaga	300
catgggaact tcggtaatag ctacatatcc tactgggctt actggggcca agggactctg	360
gtcaccgtct cctcagggtg tggtggttct ggcggcggcg gctccggtgg tggtggttct	420
cagactgttg tgactcagga accttcactc accgtatcac ctggtggaac agtcacactc	480
acttgtggct cctcgactgg ggctgttaca tctggcaact acccaaactg ggtccaacaa	540
aaaccagggtc aggcaccccg tggcttaata ggtgggacta agttcctcgc ccccggtact	600
cctgccagat tctcaggctc cctgcttgga ggcaaggctg ccctcaccct ctcaggggta	660
cagccagagg atgaggcaga atattactgt gttctatggt acagcaaccg ctgggtgttc	720
ggtggaggaa ccaaactgac tgtcctatcc ggagggtggg gctcccagggt gcagctggtc	780
cagtctggag ctgaggtgaa gaagcctgga gcgtcagtca aggtctcctg caaggctagc	840
gggtatacct tcacaaacta tggaatgaac tgggtgaagc aggtccagg acagggttta	900
aagtggatgg gctggataaa cacctacact ggagagccaa catatgctga tgacttcaag	960
ggacgggtta ccatgacttc ggatacctct accagcactg cctatgttga actccacaac	1020
ctcagaagtg atgacacggc tgtatattac tgtgcgcgct ggagttggag tgatggttac	1080
tacgtttact ttgactactg gggccaaggc actacgggtca ccgtctcctc aggtggtggt	1140
ggttctggcg gcggcggctc cgggtggtgg ggttctgaca tcgtgatgac acagtctcca	1200
gactccctga ctgtgtctct gggcgagagg accaccatca actgcaagtc cagccagagt	1260
gttttagaca gctccaagaa taagaactcc ttagcttggg accagcagaa accaggacag	1320
cctcctaaat tactcctttc ctgggcatct acgcgggaat ccgggatccc tgaccgattc	1380
agtggcagcg ggtctgggac agatttcact ctactattg acagcctgca gcctgaagat	1440
tctgcaactt actattgtca acagtctgcc cacttcccga tcacctttgg ccaagggaca	1500
cgactggaga ttaaa	1515

<210> 154

<211> 109

eolf-seql

<212> PRT
<213> artificial

<220>
<223> VL of F6A

<400> 154

Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 155
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH of F6A

<400> 155

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ile Tyr
20 25 30

eolf-seql

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Phe Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 156
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL of F6A

<400> 156

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ile Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

eolf-seql

Ser Val Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Phe Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 157

<211> 109

<212> PRT

<213> artificial

eolf-seql

<220>

<223> VL-P of F6A

<400> 157

Glu Leu Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 158

<211> 125

<212> PRT

<213> artificial

<220>

<223> VH-P of F6A

<400> 158

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ile Tyr
20 25 30

eolf-seql

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Phe Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 159
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL-P of F6A

<400> 159

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ile Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

eolf-seql

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Phe Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 160

<211> 109

<212> PRT

<213> artificial

<220>

eolf-seql

<223> VL of H2C

<400> 160

Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 161

<211> 125

<212> PRT

<213> artificial

<220>

<223> VH of H2C

<400> 161

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

eolf-seql

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 162
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL of H2C

<400> 162

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

eolf-seql

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 163
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL-P of H2C

eolf-seql

<400> 163

Glu Leu Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 164

<211> 125

<212> PRT

<213> artificial

<220>

<223> VH-P of H2C

<400> 164

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

eolf-seql

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 165
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL-P of H2C

<400> 165

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

eolf-seql

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 166
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL of H1E

<400> 166

eolf-seql

Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 167
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH of H1E

<400> 167

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Glu Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

eolf-seql

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Phe Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 168
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL of H1E

<400> 168

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Glu Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

eolf-seql

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Phe Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 169

<211> 109

<212> PRT

<213> artificial

<220>

<223> VL-P of H1E

<400> 169

Glu Leu Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

eolf-seql

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 170
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH-P of H1E

<400> 170

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Glu Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

eolf-seql

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Phe Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 171
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL-P of H1E

<400> 171

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Glu Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Phe Trp
100 105 110

eolf-seql

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 172
<211> 125
<212> PRT
<213> artificial

<220>
<223> VL of G4H

<400> 172

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

eolf-seql

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Arg Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Tyr Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 173
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH of G4H

<400> 173

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Arg Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

eolf-seql

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Tyr Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 174
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL of G4H

<400> 174

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Arg Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

eolf-seql

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Tyr Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 175

<211> 109

<212> PRT

<213> artificial

<220>

<223> VL-P of G4H

<400> 175

Glu Leu Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

eolf-seql

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 176
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH-P of G4H

<400> 176

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Arg Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

eolf-seql

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Tyr Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 177

<211> 249

<212> PRT

<213> artificial

<220>

<223> VH-VL-P of G4H

<400> 177

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Arg Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Tyr Phe
100 105 110

eolf-seql

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 178
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL of A2J

<400> 178

Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

eolf-seql

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Ala Thr Asp Met Arg Pro Ser Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 179
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH of A2J

<400> 179

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Val Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Lys Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

eolf-seql

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Trp Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 180

<211> 249

<212> PRT

<213> artificial

<220>

<223> VH-VL of A2J

<400> 180

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Val Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Lys Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Trp Trp
100 105 110

eolf-seql

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Ala
180 185 190

Thr Asp Met Arg Pro Ser Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 181
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL-P of A2J

<400> 181

Glu Leu Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

eolf-seql

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Ala Thr Asp Met Arg Pro Ser Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 182
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH-P of A2J

<400> 182

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Val Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Lys Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

eolf-seql

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Trp Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 183
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL-P of A2J

<400> 183

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Val Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Lys Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Leu Ser Trp Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

eolf-seql

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Ala
180 185 190

Thr Asp Met Arg Pro Ser Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 184
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL of E1L

<400> 184

Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

eolf-seql

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 185
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH of E1L

<400> 185

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

eolf-seql

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Thr Ser Tyr Tyr
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 186
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL of E1L

<400> 186

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Thr Ser Tyr Tyr
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

eolf-seql

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 187

<211> 109

<212> PRT

<213> artificial

<220>

<223> VL-P of E1L

<400> 187

Glu Leu Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

eolf-seql

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 188
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH-P of E1L

<400> 188

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

eolf-seql

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Thr Ser Tyr Tyr
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 189
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL-P of E1L

<400> 189

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Ser Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Thr Ser Tyr Tyr
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Val
130 135 140

eolf-seql

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 190
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL of E2M

<400> 190

Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

eolf-seql

Leu Ile Gly Ala Thr Asp Met Arg Pro Ser Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 191
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH of E2M

<400> 191

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Gly Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Glu Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Arg Asn Phe Gly Asn Ser Tyr Leu Ser Trp Phe
100 105 110

eolf-seql

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 192
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL of E2M

<400> 192

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Gly Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Glu Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Arg Asn Phe Gly Asn Ser Tyr Leu Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

eolf-seql

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Ala
180 185 190

Thr Asp Met Arg Pro Ser Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 193
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL-P of E2M

<400> 193

Glu Leu Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Ala Thr Asp Met Arg Pro Ser Gly Thr Pro Ala Arg Phe
50 55 60

eolf-seql

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 194

<211> 125

<212> PRT

<213> artificial

<220>

<223> VH-P of E2M

<400> 194

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Gly Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Glu Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Arg Asn Phe Gly Asn Ser Tyr Leu Ser Trp Phe
100 105 110

eolf-seql

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 195
<211> 249
<212> PRT
<213> artificial

<220>
<223> VH-VL-P of E2M

<400> 195

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Gly Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Glu Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Arg Asn Phe Gly Asn Ser Tyr Leu Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

eolf-seql

Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Ala
180 185 190

Thr Asp Met Arg Pro Ser Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 196
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL of F70

<400> 196

Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

eolf-seql

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 197
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH of F70

<400> 197

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Val Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Lys Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Trp Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

eolf-seql

<210> 198
 <211> 249
 <212> PRT
 <213> artificial

<220>
 <223> VH-VL of F70

<400> 198

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Val Tyr
 20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 50 55 60

Ser Val Lys Lys Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Trp Trp
 100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
 130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
 145 150 155 160

eolf-seql

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 199
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL-P of F70

<400> 199

Glu Leu Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Tyr Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

eolf-seql

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 200
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH-P of F70

<400> 200

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Val Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Lys Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Trp Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

eolf-seql

<210> 201

<211> 249

<212> PRT

<213> artificial

<220>

<223> VH-VL-P of F70

<400> 201

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Val Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Lys Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Trp Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Tyr Tyr Pro Asn
165 170 175

eolf-seql

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 202
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL of F12Q

<400> 202

Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

eolf-seql

Gln	Pro	Glu	Asp	Glu	Ala	Glu	Tyr	Tyr	Cys	Val	Leu	Trp	Tyr	Ser	Asn
				85					90					95	

Arg	Trp	Val	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu
			100					105				

<210> 203
 <211> 125
 <212> PRT
 <213> artificial

<220>
 <223> VH of F12Q

<400> 203

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
1				5					10					15	

Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Ser	Tyr
			20					25					30		

Ala	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
		35					40					45			

Ala	Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp
	50					55					60				

Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Lys	Asn	Thr
65					70					75				80	

Ala	Tyr	Leu	Gln	Met	Asn	Asn	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr
				85					90					95	

Tyr	Cys	Val	Arg	His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Val	Ser	Trp	Trp
			100					105					110		

Ala	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
							120					125

<210> 204
 <211> 249

eolf-seql

<212> PRT

<213> artificial

<220>

<223> VH-VL of F12Q

<400> 204

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
165 170 175

eolf-seql

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 205

<211> 109

<212> PRT

<213> artificial

<220>

<223> VL-P of F12Q

<400> 205

Glu Leu Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn
85 90 95

eolf-seql

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 206
<211> 125
<212> PRT
<213> artificial

<220>
<223> VH-P of F12Q

<400> 206

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 207
<211> 249
<212> PRT
<213> artificial

eolf-seql

<220>

<223> VH-VL-P of F12Q

<400> 207

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Ser Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

eolf-seql

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 208
<211> 109
<212> PRT
<213> artificial

<220>
<223> VL of I2C

<400> 208

Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105 eolf-seq1

<210> 209
 <211> 125
 <212> PRT
 <213> artificial

<220>
 <223> VH of I2C

<400> 209

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
 100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120 125

<210> 210
 <211> 249
 <212> PRT
 <213> artificial

<220>

eolf-seql

<223> VH-VL of I2C

<400> 210

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

eolf-seql

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
210 215 220

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
245

<210> 211

<211> 109

<212> PRT

<213> artificial

<220>

<223> VL-P of I2C

<400> 211

Glu Leu Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

eolf-seql

<210> 212
 <211> 125
 <212> PRT
 <213> artificial

<220>
 <223> VH-P of I2C

<400> 212

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
 100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120 125

<210> 213
 <211> 249
 <212> PRT
 <213> artificial

<220>
 <223> VH-VL-P of I2C

eolf-seql

<400> 213

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
 20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
 100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Leu Val Val
 130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
 145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
 165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
 180 185 190

Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu
 195 200 205

eolf-seql

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp
 210 215 220

Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
 225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu
 245

<210> 214
 <211> 1587
 <212> DNA
 <213> artificial

<220>
 <223> SA21-CD33 E11 HL x I2C HL (His Tag)

<400> 214
 cgcctgattg aagatatttg cctgccgcgc tggggctgcc tgtgggaaga tgatcaggtg 60
 cagctggtgc agtctggagc tgagggtgaag aagcctggag agtcagtcaa ggtctcctgc 120
 aaggctagcg ggtatacctt cacaactat ggaatgaact gggtagaagca ggctccagga 180
 cagggttttag agtggatggg ctggataaac acctacactg gagagccaac ctatgctgat 240
 aagttccagg gacgcgttac catgactacg gatacctcta ccagcactgc ctatatggaa 300
 atccgcaacc tcggagggtga tgacacggct gtatattact gtgcgcgctg gagttggagt 360
 gatggttact acgtttactt tgactactgg ggccaaggca cttcggtcac cgtctcctca 420
 ggtggtggtg gttctggcgg cggcggctcc ggtggtggtg gttctgacat cgtgatgaca 480
 cagtctccag actccctgac tgtgtctctg ggcgagagga ccaccatcaa ctgcaagtcc 540
 agccagagtg ttttagacag ctccacgaat aagaactcct tagcttggtg ccagcagaaa 600
 ccaggacagc ctctaaatt actcctttcc tgggcatcta cgcgggaatc cgggatccct 660
 gaccgattca gtggcagcgg gtctgggaca gatttcactc tcactattga cagcccgcag 720
 cctgaagatt ctgcaactta ctattgtcaa cagtctgccc acttcccgat cacctttggc 780
 caagggacac gactggagat taaatccgga ggtggtggct ccgaggtgca gctggtcgag 840
 tctggaggag gattggtgca gcctggaggg tcattgaaac tctcatgtgc agcctctgga 900

eolf-seql

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ttcaccttca ataagtacgc catgaactgg gtccgccagg ctccaggaaa gggtttggaa    960
tgggttgctc gcataagaag taaatataat aattatgcaa catattatgc cgattcagtg    1020
aaagacaggt tcaccatctc cagagatgat tcaaaaaaca ctgcctatct acaaatgaac    1080
aacttgaaaa ctgaggacac tgccgtgtac tactgtgtga gacatgggaa cttcggtaat    1140
agctacatat cctactgggc ttactggggc caagggactc tggtcaccgt ctcctcaggt    1200
gggtggtggtt ctggcggcgg cggctccggt ggtggtggtt ctcagactgt tgtgactcag    1260
gaaccttcac tcaccgtatc acctgggtgga acagtcacac tcacttgtgg ctcctcgact    1320
ggggctgtta catctggcaa ctacccaaac tgggtccaac aaaaaccagg tcaggcaccc    1380
cgtggtctaa taggtgggac taagttcctc gcccccggtc ctcctgccag attctcaggc    1440
tccctgcttg gaggcaaggc tgccctcacc ctctcagggg tacagccaga ggatgaggca    1500
gaatattact gtgttctatg gtacagcaac cgctgggtgt tcggtggagg aaccaaactg    1560
actgtcctac atcaccatca ccatcac                                     1587

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<210> 215
 <211> 529
 <212> PRT
 <213> artificial

<220>
 <223> SA21-CD33 E11 HL x I2C HL H6

<400> 215

Arg	Leu	Ile	Glu	Asp	Ile	Cys	Leu	Pro	Arg	Trp	Gly	Cys	Leu	Trp	Glu
1				5					10					15	

Asp	Asp	Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro
		20						25					30		

Gly	Glu	Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr
		35					40					45			

Asn	Tyr	Gly	Met	Asn	Trp	Val	Lys	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu
	50					55					60				

eolf-seq1

Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp
65 70 75 80

Lys Phe Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr
85 90 95

Ala Tyr Met Glu Ile Arg Asn Leu Gly Gly Asp Asp Thr Ala Val Tyr
100 105 110

Tyr Cys Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp
115 120 125

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr
145 150 155 160

Gln Ser Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile
165 170 175

Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn
180 185 190

Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu
195 200 205

Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser
210 215 220

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Pro Gln
225 230 235 240

Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro
245 250 255

Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly
260 265 270

eolf-seq1

Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
275 280 285

Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn
290 295 300

Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
305 310 315 320

Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr
325 330 335

Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys
340 345 350

Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala
355 360 365

Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser
370 375 380

Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
385 390 395 400

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr
405 410 415

Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val
420 425 430

Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr
435 440 445

Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile
450 455 460

Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly
465 470 475 480

eolf-seql

Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro
485 490 495

Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp
500 505 510

Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu His His His His His
515 520 525

His

<210> 216
<211> 1575
<212> DNA
<213> artificial

<220>
<223> SA25-CD33 E11 HL x I2C HL with His tag

<400> 216
gaggacatct gcctgccag atggggctgc ctgtgggagg accaggtgca gctgggtgcag 60
tctggagctg aggtgaagaa gcctggagag tcagtcaagg tctcctgcaa ggctagcggg 120
tataccttca caaactatgg aatgaactgg gtgaagcagg ctccaggaca gggtttagag 180
tggatgggct ggataaacac ctacactgga gagccaacct atgctgataa gttccaggga 240
cgcgttacca tgactacgga tacctctacc agcactgcct atatggaaat ccgcaacctc 300
ggaggtgatg acacggctgt atattactgt gcgcgctgga gttggagtga tggttactac 360
gtttactttg actactgggg ccaaggcact tcggtcaccg tctcctcagg tgggtggtggt 420
tctggcggcg gcggctccgg tgggtggtggt tctgacatcg tgatgacaca gtctccagac 480
tccctgactg tgtctctggg cgagaggacc accatcaact gcaagtccag ccagagtgtt 540
ttagacagct ccacgaataa gaactcctta gcttggtacc agcagaaacc aggacagcct 600
cctaaattac tcctttcctg ggcatctacg cgggaatccg ggatccctga ccgattcagt 660
ggcagcgggt ctgggacaga tttcactctc actattgaca gcccgcagcc tgaagattct 720
gcaacttact attgtcaaca gtctgcccac ttcccgatca cttttggcca aggacacga 780
ctggagatta aatccggagg tgggtggctcc gaggtgcagc tggtcgagtc tggaggagga 840

eolf-seql

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ttggtgcagc ctggagggtc attgaaactc tcatgtgcag cctctggatt caccttcaat    900
aagtacgcca tgaactgggt ccgccaggct ccaggaaagg gtttggaatg ggttgctcgc    960
ataagaagta aatataataa ttatgcaaca tattatgccg attcagtgaag agacaggttc   1020
accatctcca gagatgattc aaaaaacact gcctatctac aaatgaacaa cttgaaaact   1080
gaggacactg ccgtgtacta ctgtgtgaga catgggaact tcggtaatag ctacatatcc   1140
tactgggctt actggggcca agggactctg gtcaccgtct cctcagggtg tggtggttct   1200
ggcggcggcg gctccggtgg tggtggttct cagactgttg tgactcagga accttcactc   1260
accgtatcac ctggtggaac agtcacactc acttgtggct cctcgactgg ggctgttaca   1320
tctggcaact acccaaactg ggtccaacaa aaaccaggctc aggcaccccg tggcttaata   1380
ggtgggacta agttcctcgc ccccggtact cctgccagat tctcaggctc cctgcttggg   1440
ggcaaggctg ccctcacctc ctcaggggta cagccagagg atgaggcaga atattactgt   1500
gttctatggt acagcaaccg ctgggtgttc ggtggaggaa ccaaactgac tgtcctacat   1560
caccatcacc atcac                                     1575

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<210> 217
 <211> 525
 <212> PRT
 <213> artificial

<220>
 <223> SA25-CD33 E11 HL x I2C HL H6

<400> 217

Glu Asp Ile Cys Leu Pro Arg Trp Gly Cys Leu Trp Glu Asp Gln Val
 1 5 10 15

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu Ser Val
 20 25 30

Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Met
 35 40 45

Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp
 50 55 60

eolf-seql

Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe Gln Gly
65 70 75 80

Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu
85 90 95

Ile Arg Asn Leu Gly Gly Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg
100 105 110

Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Ser Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser Pro Asp
145 150 155 160

Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys Lys Ser
165 170 175

Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu Ala Trp
180 185 190

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser Trp Ala
195 200 205

Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser
210 215 220

Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Pro Gln Pro Glu Asp Ser
225 230 235 240

Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr Phe Gly
245 250 255

Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val
260 265 270

eolf-seql

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
275 280 285

Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met
290 295 300

Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg
305 310 315 320

Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val
325 330 335

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr
340 345 350

Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
355 360 365

Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr
370 375 380

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
385 390 395 400

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln
405 410 415

Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys
420 425 430

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val
435 440 445

Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys
450 455 460

Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly
465 470 475 480

eolf-seql

Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala
485 490 495

Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly
500 505 510

Gly Thr Lys Leu Thr Val Leu His His His His His His
515 520 525

<210> 218
<211> 1596
<212> DNA
<213> artificial

<220>
<223> SA08-CD33 E11 HL x I2C HL with His tag

<400> 218
cagggcctga tcggcgacat ctgcctgccc agatggggct gcctgtgggg cgactccgtg 60
aaacaggtgc agctggtgca gtctggagct gaggtgaaga agcctggaga gtcagtcaag 120
gtctcctgca aggctagcgg gtataccttc acaaactatg gaatgaactg ggtgaagcag 180
gctccaggac agggtttaga gtggatgggc tggataaaca cctacactgg agagccaacc 240
tatgctgata agttccaggg acgcgttacc atgactacgg atacctctac cagcactgcc 300
tatatggaaa tccgcaacct cggaggtgat gacacggctg tatattactg tgcgcgctgg 360
agttggagtg atggttacta cgtttacttt gactactggg gccaaggcac ttcggtcacc 420
gtctcctcag gtggtggtgg ttctggcggc ggcggtccg gtggtggtgg ttctgacatc 480
gtgatgacac agtctccaga ctccctgact gtgtctctgg gcgagaggac caccatcaac 540
tgcaagtcca gccagagtgt tttagacagc tccacgaata agaactcctt agcttggtac 600
cagcagaaac caggacagcc tcctaaatta ctcttttctt gggcatctac gcgggaatcc 660
gggatccctg accgattcag tggcagcggg tctgggacag atttcactct cactattgac 720
agcccgcagc ctgaagattc tgcaacttac tattgtcaac agtctgcca cttcccgatc 780
acctttggcc aaggacacg actggagatt aaatccggag gtggtggctc cgaggtgcag 840
ctggtcgagt ctggaggagg attggtgcag cctggagggt cattgaaact ctcatgtgca 900

eolf-seql

gcctctggat tcaccttcaa taagtacgcc atgaactggg tccgccaggc tccaggaaag 960
 gggttggaat gggttgctcg cataagaagt aaatataata attatgcaac atattatgcc 1020
 gattcagtga aagacagggt caccatctcc agagatgatt caaaaaacac tgcctatcta 1080
 caaatgaaca acttgaaaac tgaggacact gccgtgtact actgtgtgag acatgggaac 1140
 ttcggttaata gctacatatc ctactgggct tactggggcc aagggactct ggtcaccgtc 1200
 tcctcagggtg gtggtggttc tggcggcggc ggctccgggtg gtggtggttc tcagactggt 1260
 gtgactcagg aaccttcact caccgtatca cctgggtggaa cagtcacact cacttgtggc 1320
 tcctcgactg gggctgttac atctggcaac tacccaaact gggccaaca aaaaccagggt 1380
 caggcacccc gtggtctaata aggtgggact aagttcctcg ccccggtac tcctgccaga 1440
 ttctcaggct ccctgcttgg aggcaaggct gccctcacc tctcaggggt acagccagag 1500
 gatgaggcag aatattactg tgttctatgg tacagcaacc gctgggtggt cggtggagga 1560
 accaaactga ctgtcctaca tcaccatcac catcac 1596

<210> 219
 <211> 532
 <212> PRT
 <213> artificial

<220>
 <223> SA08-CD33 E11 HL x I2C HL H6

<400> 219

Gln Gly Leu Ile Gly Asp Ile Cys Leu Pro Arg Trp Gly Cys Leu Trp
 1 5 10 15

Gly Asp Ser Val Lys Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
 20 25 30

Lys Lys Pro Gly Glu Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
 35 40 45

Thr Phe Thr Asn Tyr Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln
 50 55 60

eolf-seql

Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr
65 70 75 80

Tyr Ala Asp Lys Phe Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Ile Arg Asn Leu Gly Gly Asp Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val
115 120 125

Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
145 150 155 160

Val Met Thr Gln Ser Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg
165 170 175

Thr Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr
180 185 190

Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
195 200 205

Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp
210 215 220

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp
225 230 235 240

Ser Pro Gln Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala
245 250 255

His Phe Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser
260 265 270

eolf-seql

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
275 280 285

Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe
290 295 300

Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys
305 310 315 320

Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
325 330 335

Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp
340 345 350

Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu
355 360 365

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser
370 375 380

Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
385 390 395 400

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
405 410 415

Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
420 425 430

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser
435 440 445

Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg
450 455 460

Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg
465 470 475 480

eolf-seql

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly
485 490 495

Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser
500 505 510

Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu His His
515 520 525

His His His His
530

<210> 220
<211> 1569
<212> DNA
<213> artificial

<220>
<223> SA21-CD33 E11 HL x I2C HL

<400> 220
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cagctggtgc agtctggagc tgaggatgaag aagcctggag agtcagtcaa ggtctcctgc 120
aaggctagcg ggtatacctt cacaactat ggaatgaact gggatgaagca ggctccagga 180
cagggttttag agtggatggg ctggataaac acctacactg gagagccaac ctatgctgat 240
aagttccagg gacgcgttac catgactacg gatacctcta ccagcactgc ctatatggaa 300
atccgcaacc tcggagggtga tgacacggct gtatattact gtgcgcgctg gagttggagt 360
gatggttact acgtttactt tgactactgg ggccaaggca cttcggtcac cgtctcctca 420
ggatgggtggg gttctggcgg cggcggctcc ggtgggtggg gttctgacat cgtgatgaca 480
cagtctccag actccctgac tgtgtctctg ggcgagagga ccaccatcaa ctgcaagtcc 540
agccagagtg ttttagacag ctccacgaat aagaactcct tagcttggtg ccagcagaaa 600
ccaggacagc ctctaaatt actcctttcc tgggcatcta cgcgggaatc cgggatccct 660
gaccgattca gtggcagcgg gtctgggaca gatttcactc tcactattga cagcccgcag 720
cctgaagatt ctgcaactta ctattgtcaa cagtctgccc acttcccgat cacctttggc 780
caaggacac gactggagat taaatccgga ggtgggtggc ccgaggtgca gctggtcgag 840

eolf-seql

tctggaggag gattggtgca gcctggaggg tcattgaaac tctcatgtgc agcctctgga 900
 ttcaccttca ataagtacgc catgaactgg gtccgccagg ctccaggaaa gggtttgaa 960
 tgggttgctc gcataagaag taaatataat aattatgcaa catattatgc cgattcagt 1020
 aaagacaggt tcaccatctc cagagatgat tcaaaaaaca ctgcctatct acaaatgaac 1080
 aacttgaaaa ctgaggacac tgccgtgtac tactgtgtga gacatgggaa cttcggtaat 1140
 agctacatat cctactgggc ttactggggc caagggactc tggtcaccgt ctctcaggt 1200
 ggtggtggtt ctggcggcgg cggctccggt ggtggtggtt ctcagactgt tgtgactcag 1260
 gaaccttcac tcaccgtatc acctgggtgga acagtcacac tcaattgtgg ctctcgact 1320
 ggggctgtta catctggcaa ctacccaaac tgggtccaac aaaaaccagg tcaggcaccc 1380
 cgtggtctaa taggtgggac taagttcctc gccccggta ctctgccag attctcaggc 1440
 tccctgcttg gaggcaaggc tgccctcacc ctctcagggg tacagccaga ggatgaggca 1500
 gaatattact gtgttctatg gtacagcaac cgctgggtgt tcggtggagg aaccaaactg 1560
 actgtccta 1569

<210> 221
 <211> 523
 <212> PRT
 <213> artificial

<220>
 <223> SA21-CD33 E11 HL x I2C HL

<400> 221

Arg Leu Ile Glu Asp Ile Cys Leu Pro Arg Trp Gly Cys Leu Trp Glu
 1 5 10 15

Asp Asp Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro
 20 25 30

Gly Glu Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr
 35 40 45

Asn Tyr Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu
 50 55 60

eolf-seql

Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp
65 70 75 80

Lys Phe Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr
85 90 95

Ala Tyr Met Glu Ile Arg Asn Leu Gly Gly Asp Asp Thr Ala Val Tyr
100 105 110

Tyr Cys Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp
115 120 125

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr
145 150 155 160

Gln Ser Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile
165 170 175

Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn
180 185 190

Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu
195 200 205

Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser
210 215 220

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Pro Gln
225 230 235 240

Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro
245 250 255

Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly
260 265 270

eolf-seql

Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
275 280 285

Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn
290 295 300

Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
305 310 315 320

Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr
325 330 335

Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys
340 345 350

Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala
355 360 365

Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser
370 375 380

Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
385 390 395 400

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr
405 410 415

Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val
420 425 430

Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr
435 440 445

Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile
450 455 460

Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly
465 470 475 480

eolf-seql

Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro
485 490 495

Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp
500 505 510

Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
515 520

<210> 222
<211> 1557
<212> DNA
<213> artificial

<220>
<223> SA25-CD33 E11 HL x I2C HL

<400> 222
gaggacatct gcctgcccag atggggctgc ctgtgggagg accaggtgca gctggtgcag 60
tctggagctg aggtgaagaa gcctggagag tcagtcaagg tctcctgcaa ggctagcggg 120
tataccttca caaactatgg aatgaactgg gtgaagcagg ctccaggaca gggtttagag 180
tggatgggct ggataaacac ctacactgga gagccaacct atgctgataa gttccaggga 240
cgcgttacca tgactacgga tacctctacc agcactgcct atatggaaat ccgcaacctc 300
ggaggtgatg acacggctgt atattactgt gcgcgctgga gttggagtga tggttactac 360
gtttactttg actactgggg ccaaggcact tcggtcaccg tctcctcagg tgggtggtggt 420
tctggcggcg gcggctccgg tgggtggtggt tctgacatcg tgatgacaca gtctccagac 480
tccctgactg tgtctctggg cgagaggacc accatcaact gcaagtccag ccagagtgtt 540
ttagacagct ccacgaataa gaactcctta gcttggtacc agcagaaacc aggacagcct 600
cctaaattac tcctttcctg ggcatctacg cgggaatccg ggatccctga ccgattcagt 660
ggcagcgggt ctgggacaga ttctactctc actattgaca gcccgcagcc tgaagattct 720
gcaacttact attgtcaaca gtctgcccac ttcccgatca cttttggcca aggacacga 780
ctggagatta aatccggagg tgggtggtcc gaggtgcagc tggtcgagtc tggaggagga 840
ttggtgcagc ctggagggtc attgaaactc tcatgtgcag cctctggatt caccttcaat 900

eolf-seql

aagtacgcca tgaactgggt ccgccaggct ccaggaaaagg gtttggaatg ggttgctcgc 960
 ataagaagta aatataataa ttatgcaaca tattatgccg attcagtgaag agacagggttc 1020
 accatctcca gagatgattc aaaaaacact gcctatctac aaatgaacaa cttgaaaact 1080
 gaggacactg ccgtgtacta ctgtgtgaga catgggaact tcggtaatag ctacatatcc 1140
 tactgggctt actggggcca agggactctg gtcaccgtct cctcagggtg tggtgggttct 1200
 ggcggcggcg gctccgggtg tggtgggttct cagactgttg tgactcagga accttcactc 1260
 accgtatcac ctggtggaac agtcacactc acttgtggct cctcgactgg ggctgttaca 1320
 tctggcaact acccaaactg ggtccaacaa aaaccagggtc aggcaccccg tggtctaata 1380
 ggtgggacta agttcctcgc ccccggtact cctgccagat tctcaggctc cctgcttgga 1440
 ggcaaggctg ccctcaccct ctcaggggta cagccagagg atgaggcaga atattactgt 1500
 gttctatggg acagcaaccg ctgggtgttc ggtggaggaa ccaaactgac tgtccta 1557

<210> 223
 <211> 519
 <212> PRT
 <213> artificial

<220>
 <223> SA25-CD33 E11 HL x I2C HL

<400> 223

Glu	Asp	Ile	Cys	Leu	Pro	Arg	Trp	Gly	Cys	Leu	Trp	Glu	Asp	Gln	Val
1				5				10						15	

Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Glu	Ser	Val
			20					25					30		

Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Asn	Tyr	Gly	Met
		35					40					45			

Asn	Trp	Val	Lys	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	Gly	Trp
50						55					60				

Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	Ala	Asp	Lys	Phe	Gln	Gly
65					70					75				80	

eolf-seql

Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu
85 90 95

Ile Arg Asn Leu Gly Gly Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg
100 105 110

Trp Ser Trp Ser Asp Gly Tyr Tyr Val Tyr Phe Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Ser Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser Pro Asp
145 150 155 160

Ser Leu Thr Val Ser Leu Gly Glu Arg Thr Thr Ile Asn Cys Lys Ser
165 170 175

Ser Gln Ser Val Leu Asp Ser Ser Thr Asn Lys Asn Ser Leu Ala Trp
180 185 190

Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Leu Ser Trp Ala
195 200 205

Ser Thr Arg Glu Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser
210 215 220

Gly Thr Asp Phe Thr Leu Thr Ile Asp Ser Pro Gln Pro Glu Asp Ser
225 230 235 240

Ala Thr Tyr Tyr Cys Gln Gln Ser Ala His Phe Pro Ile Thr Phe Gly
245 250 255

Gln Gly Thr Arg Leu Glu Ile Lys Ser Gly Gly Gly Gly Ser Glu Val
260 265 270

Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu
275 280 285

eolf-seql

Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr Ala Met
290 295 300

Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg
305 310 315 320

Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val
325 330 335

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Ala Tyr
340 345 350

Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys
355 360 365

Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr
370 375 380

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
385 390 395 400

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln
405 410 415

Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys
420 425 430

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val
435 440 445

Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys
450 455 460

Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly
465 470 475 480

Gly Lys Ala Ala Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala
485 490 495

eolf-seql

Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Gly
500 505 510

Gly Thr Lys Leu Thr Val Leu
515

<210> 224
<211> 1578
<212> DNA
<213> artificial

<220>
<223> SA08-CD33 E11 HL x I2C HL

<400> 224
cagggcctga tcggcgacat ctgcctgccc agatggggct gcctgtgggg cgactccgtg 60
aaacaggtgc agctgggtgca gtctggagct gaggtgaaga agcctggaga gtcagtcaag 120
gtctcctgca aggctagcgg gtataccttc acaaactatg gaatgaactg ggtgaagcag 180
gctccaggac agggttttaga gtggatgggc tggataaaca cctacactgg agagccaacc 240
tatgctgata agttccaggg acgcgttacc atgactacgg atacctctac cagcactgcc 300
tatatggaaa tccgcaacct cggaggtgat gacacggctg tatattactg tgcgcgctgg 360
agttggagtg atggttacta cgtttacttt gactactggg gccaaaggcac ttcggtcacc 420
gtctcctcag gtggtgggtgg ttctggcggc ggcggtctccg gtggtgggtgg ttctgacatc 480
gtgatgacac agtctccaga ctccctgact gtgtctctgg gcgagaggac caccatcaac 540
tgcaagtcca gccagagtgt tttagacagc tccacgaata agaactcctt agcttggtac 600
cagcagaaac caggacagcc tcctaaatta ctcttttcct gggcatctac gcgggaatcc 660
gggatccctg accgattcag tggcagcggg tctgggacag atttcactct cactattgac 720
agcccgagc ctgaagattc tgcaacttac tattgtcaac agtctgcca cttcccgatc 780
acctttggcc aagggacacg actggagatt aaatccggag gtggtggctc cgaggtgcag 840
ctggctgagt ctggaggagg attggtgcag cctggagggt cattgaaact ctcatgtgca 900
gcctctggat tcaccttcaa taagtacgcc atgaactggg tccgccaggc tccaggaaaag 960
ggtttggaaat gggttgctcg cataagaagt aaatataata attatgcaac atattatgcc 1020

eolf-seql

gattcagtga aagacaggtt caccatctcc agagatgatt caaaaaacac tgcctatcta 1080
 caaatgaaca acttgaaaac tgaggacact gccgtgtact actgtgtgag acatgggaac 1140
 ttcggttaata gctacatatc ctactgggct tactggggcc aagggactct ggtcaccgtc 1200
 tcctcaggtg gtggtgggtc tggcggcggc ggctccggtg gtggtgggtc tcagactggt 1260
 gtgactcagg aaccttcact caccgtatca cctgggtggaa cagtcacact cacttgtggc 1320
 tcctcgactg gggctgttac atctggcaac tacccaaact gggccaaca aaaaccaggt 1380
 caggcacccc gtggtctaata aggtgggact aagttcctcg cccccgtac tcctgccaga 1440
 ttctcaggct ccctgcttgg aggcaaggct gccctcacc tctcaggggt acagccagag 1500
 gatgaggcag aatattactg tgttctatgg tacagcaacc gctgggtgtt cggtggagga 1560
 accaaactga ctgtccta 1578

<210> 225
 <211> 526
 <212> PRT
 <213> artificial

<220>
 <223> SA08-CD33 E11 HL x I2C HL

<400> 225

Gln Gly Leu Ile Gly Asp Ile Cys Leu Pro Arg Trp Gly Cys Leu Trp
 1 5 10 15

Gly Asp Ser Val Lys Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
 20 25 30

Lys Lys Pro Gly Glu Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
 35 40 45

Thr Phe Thr Asn Tyr Gly Met Asn Trp Val Lys Gln Ala Pro Gly Gln
 50 55 60

Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr
 65 70 75 80

eolf-seq1

Tyr Ala Asp Lys Phe Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Ile Arg Asn Leu Gly Gly Asp Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Trp Ser Trp Ser Asp Gly Tyr Tyr Val
115 120 125

Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
145 150 155 160

Val Met Thr Gln Ser Pro Asp Ser Leu Thr Val Ser Leu Gly Glu Arg
165 170 175

Thr Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Asp Ser Ser Thr
180 185 190

Asn Lys Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
195 200 205

Lys Leu Leu Leu Ser Trp Ala Ser Thr Arg Glu Ser Gly Ile Pro Asp
210 215 220

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp
225 230 235 240

Ser Pro Gln Pro Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Ala
245 250 255

His Phe Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Ser
260 265 270

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
275 280 285

eolf-seq1

Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe
290 295 300

Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys
305 310 315 320

Gly Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
325 330 335

Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp
340 345 350

Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu
355 360 365

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser
370 375 380

Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
385 390 395 400

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
405 410 415

Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
420 425 430

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser
435 440 445

Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg
450 455 460

Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg
465 470 475 480

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly
485 490 495

eolf-seql

Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser
500 505 510

Asn Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
515 520 525

<210> 226
<211> 1533
<212> DNA
<213> artificial

<220>
<223> CD33 E11 HL x I2C HL (His Tag)

<400> 226
cagggtgcagc tgggtgcagtc tggagctgag gtgaagaagc ctggagagtc agtcaaggct 60
tcctgcaagg ctagcgggta taccttcaca aactatggaa tgaactgggt gaagcaggct 120
ccaggacagg gtttagagtg gatgggctgg ataaacacct aactggaga gccaacctat 180
gctgataagt tccaggagcg cgttaccatg actacggata cctctaccag cactgcctat 240
atggaaatcc gcaacctcgg aggtgatgac acggctgtat attactgtgc gcgctggagt 300
tggagtgatg gttactacgt ttactttgac tactggggcc aaggcacttc ggtcaccgtc 360
tcctcagggtg gtgggtggttc tggcggcggc ggctccgggtg gtgggtggttc tgacatcgtg 420
atgacacagt ctccagactc cctgactgtg tctctgggcg agaggaccac catcaactgc 480
aagtccagcc agagtgtttt agacagctcc acgaataaga actccttagc ttggtaccag 540
cagaaaccag gacagcctcc taaattactc ctttcctggg catctacgcg ggaatccggg 600
atccctgacc gattcagtg gacgggtct gggacagatt tcactctcac tattgacagc 660
ccgcagcctg aagattctgc aacttactat tgtcaacagt ctgcccactt cccgatcacc 720
tttggccaag ggacacgact ggagattaaa tccggagggtg gtggctccga ggtgcagctg 780
gtcgagtctg gaggaggatt ggtgcagcct ggagggtcat tgaaactctc atgtgcagcc 840
tctggattca cttcaataa gtacgccatg aactgggtcc gccaggctcc aggaaagggt 900
ttggaatggg ttgctcgcac aagaagtaaa tataataatt atgcaacata ttatgccgat 960
tcagtgaaag acaggttcac catctccaga gatgattcaa aaaacactgc ctatctacaa 1020
atgaacaact tgaaaactga ggacactgcc gtgtactact gtgtgagaca tgggaacttc 1080

eolf-seql

ggtaatagct acatatccta ctgggcttac tggggccaag ggactctggt caccgtctcc 1140
tcaggtggtg gtggttctgg cggcggcggc tccggtggtg gtggttctca gactgttggt 1200
actcaggaac cttcactcac cgtatcacct ggtggaacag tcacactcac ttgtggctcc 1260
tcgactgggg ctgttacatc tggcaactac ccaaactggg tccaacaaaa accaggtcag 1320
gcaccccgtg gtctaataagg tgggactaag ttcctcgccc ccggtactcc tgccagattc 1380
tcaggctccc tgcttggagg caaggctgcc ctcaccctct caggggtaca gccagaggat 1440
gaggcagaat attactgtgt tctatggtac agcaaccgct ggggtgttcgg tggaggaacc 1500
aaactgactg tcctacatca ccatcaccat cac 1533

<210> 227
<211> 511
<212> PRT
<213> artificial

<220>
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Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Lys Phe
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Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn Arg Trp Val Phe
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Gly Gly Gly Thr Lys Leu Thr Val Leu His His His His His His
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Claims

1. A pharmaceutical composition comprising a CD33 targeting compound and at least one epigenetic factor, wherein
 - (a) the CD33 targeting compound is a bispecific construct comprising a first binding domain specifically binding to CD33 and a second binding domain specifically binding to CD3; and
 - (b) the at least one epigenetic factor is selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors, hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone methyltransferase (HMT) inhibitors and ATRA (All Trans-retinoic acid).
2. The pharmaceutical composition of claim 1, wherein the at least one epigenetic factor is selected from the group comprising
 - (a) a histone deacetylase (HDAC) inhibitor selected from the group consisting of panobinostat, vorinostat, romidepsin, N-acetyldinaline, belinostat, givinostat, entinostat, mocetinostat, EVP-0334, SRT501, CUDC-101, Quisinostat, abexinostat, LAQ824, and valproic acid;
 - (b) a DNA methyltransferase (DNMT) I inhibitor selected from the group consisting of 5-azacitidine, decitabine, hydralazine, zebularine, procainamide, (-)-epigallocatechin-3-gallate, MG98, RG108, and SGI-110; and
 - (c) a histone methyltransferase (HMT) inhibitor selected from the group consisting of LSD1 (KDM1A) demethylase inhibitor, and chaetocin.
3. The pharmaceutical composition of claim 1 or 2, wherein
 - (a) the epigenetic factor is administered prior to the administration of the CD33 targeting compound;
 - (b) the epigenetic factor is administered subsequent to the administration of the CD33 targeting compound; or
 - (c) the epigenetic factor and the CD33 targeting compound are administered simultaneously.
4. The pharmaceutical composition of any of claims 1 to 3, wherein a first dose of the epigenetic factor is administered prior to the start of the administration of the CD33 targeting compound.

5. The pharmaceutical composition of claim 4, wherein the administration of the epigenetic factor is continued during the administration of the CD33 targeting compound.
6. The pharmaceutical composition of any of claims 1 to 5, wherein the bispecific construct is a bispecific antibody construct.
7. The pharmaceutical composition of claim 6, wherein the bispecific antibody construct is a bispecific single chain antibody construct.
8. The pharmaceutical composition of claim 6 or 7, wherein the bispecific antibody construct binds to human and cynomolgous CD3 and human and cynomolgous CD33.
9. The pharmaceutical composition of any of claims 6 to 8, wherein the bispecific antibody construct comprises
 - a first binding domain specifically binding to CD33 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 6, 24, 42, 60, 78, 96, 114 and 132 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 1, 19, 37, 55, 73, 91, 109 and 127; and
 - a second binding domain specifically binding to CD3 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 154, 157, 160, 163, 166, 169 and 172 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 155, 158, 161, 164, 167, 170 and 173.
10. The pharmaceutical composition of claim 9, wherein the bispecific antibody construct comprises an amino acid sequence as depicted in any of SEQ ID NOs: 13, 15, 17, 31, 33, 35, 49, 51, 53, 67, 69, 71, 85, 87, 89, 103, 105, 107, 121, 123, 125, 139, 141, 143, 148, 150, 152, 215, 217, 219, 221, 223, 225 and 227.
11. The pharmaceutical composition of any of claims 1 to 10 for the treatment of a myeloid leukemia.
12. The pharmaceutical composition of claim 11, wherein the myeloid leukemia is selected from the group consisting of acute myeloblastic leukemia, chronic neutrophilic leukemia, myeloid dendritic cell leukemia, accelerated phase chronic myelogenous leukemia, acute myelomonocytic leukemia, juvenile myelomonocytic

leukemia, chronic myelomonocytic leukemia, acute basophilic leukemia, acute eosinophilic leukemia, chronic eosinophilic leukemia, Acute megakaryoblastic leukemia, essential thrombocytosis, acute erythroid leukemia, polycythemia vera, myelodysplastic syndrome, acute panmyelosis, myeloid sarcoma, and acute biphenotypic leukaemia.

13. An epigenetic factor for use in the amelioration and/or treatment of a myeloid leukemia, wherein the epigenetic factor increases the responsiveness of a patient to a CD33 targeting compound, wherein
 - (a) the CD33 targeting compound is a bispecific construct comprising a first binding domain specifically binding to CD33 and a second binding domain specifically binding to CD3; and
 - (b) the at least one epigenetic factor is selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors, hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone methyltransferase (HMT) inhibitors and ATRA (All Trans-retinoic acid).
14. The epigenetic factor of claim 13, wherein the epigenetic factor is selected from the group comprising
 - (a) a histone deacetylase (HDAC) inhibitor selected from the group consisting of panobinostat, vorinostat, romidepsin, N-acetyldinaline, belinostat, givinostat, entinostat, mocetinostat, EVP-0334, SRT501, CUDC-101, Quisinostat, abexinostat, LAQ824, and valproic acid;
 - (b) a DNA methyltransferase (DNMT) I inhibitor selected from the group consisting of 5-azacitidine, decitabine, hydralazine, zebularine, procainamide, (-)-epigallocatechin-3-gallate, MG98, RG108, and SGI-110; and
 - (c) a histone methyltransferase (HMT) inhibitor selected from the group consisting of LSD1 (KDM1A) demethylase inhibitor, and chaetocin.
15. The epigenetic factor of claim 13 or 14, wherein
 - (a) the epigenetic factor is administered prior to the administration of the CD33 targeting compound;
 - (b) the epigenetic factor is administered subsequent to the administration of the CD33 targeting compound; or
 - (c) the epigenetic factor and the CD33 targeting compound are administered simultaneously.

16. The epigenetic factor of any of claims 13 to 15, wherein a first dose of the epigenetic factor is administered prior to the start of the administration of the CD33 targeting compound.
17. The epigenetic factor of claim 16, wherein the administration of the epigenetic factor is continued during the administration of the CD33 targeting compound.
18. The epigenetic factor of any of claim 13 to 17, wherein the bispecific construct is a bispecific antibody construct.
19. The epigenetic factor of claim 18, wherein the bispecific antibody construct is a bispecific single chain antibody construct.
20. The epigenetic factor of claim 18 or 19, wherein the bispecific antibody construct binds to human and cynomolgous CD3 and CD33.
21. The epigenetic factor of any of claim 18 to 20, wherein the bispecific antibody construct comprises
 - a first binding domain specifically binding to CD33 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 6, 24, 42, 60, 78, 96, 114 and 132 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 1, 19, 37, 55, 73, 91, 109 and 127; and
 - a second binding domain specifically binding to CD3 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 154, 157, 160, 163, 166, 169 and 172 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 155, 158, 161, 164, 167, 170 and 173.
22. The epigenetic factor of claim 21, wherein the bispecific antibody construct comprises an amino acid sequence as depicted in any of SEQ ID NOs: 13, 15, 17, 31, 33, 35, 49, 51, 53, 67, 69, 71, 85, 87, 89, 103, 105, 107, 121, 123, 125, 139, 141, 143, 148, 150, 152, 215, 217, 219, 221, 223, 225 and 227.
23. The epigenetic factor of any of claims 13 to 22, wherein the myeloid leukemia is selected from the group consisting of acute myeloblastic leukemia, chronic neutrophilic leukemia, myeloid dendritic cell leukemia, accelerated phase chronic myelogenous leukemia, acute myelomonocytic leukemia, juvenile myelomonocytic leukemia, chronic myelomonocytic leukemia, acute basophilic leukemia, acute

eosinophilic leukemia, chronic eosinophilic leukemia, Acute megakaryoblastic leukemia, essential thrombocytosis, acute erythroid leukemia, polycythemia vera, myelodysplastic syndrome, acute panmyelosis, myeloid sarcoma, and acute biphenotypic leukaemia.

24. An use of at least one an epigenetic factor for increasing the responsiveness of a myeloid leukemia patient to a treatment with a CD33 targeting compound, wherein
 - (a) the CD33 targeting compound is a bispecific construct comprising a first binding domain specifically binding to CD33 and a second binding domain specifically binding to CD3; and
 - (b) the at least one epigenetic factor is selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors, hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone methyltransferase (HMT) inhibitors and ATRA (All Trans-retinoic acid).
25. The use of claim 24, wherein the at least one epigenetic factor is selected from the group comprising
 - (a) a histone deacetylase (HDAC) inhibitor selected from the group consisting of panobinostat, vorinostat, romidepsin, N-acetyldinaline, belinostat, givinostat, entinostat, mocetinostat, EVP-0334, SRT501, CUDC-101, Quisinostat, abexinostat, LAQ824, and valproic acid;
 - (b) a DNA methyltransferase (DNMT) I inhibitor selected from the group consisting of 5-azacitidine, decitabine, hydralazine, zebularine, procainamide, (-)-epigallocatechin-3-gallate, MG98, RG108, and SGI-110; and
 - (c) a histone methyltransferase (HMT) inhibitor selected from the group consisting of LSD1 (KDM1A) demethylase inhibitor, and chaetocin.
26. The use of claim 24 or 25, wherein
 - (a) the epigenetic factor is administered prior to the administration of the CD33 targeting compound;
 - (b) the epigenetic factor is administered subsequent to the administration of the CD33 targeting compound; or
 - (c) the epigenetic factor and the CD33 targeting compound are administered simultaneously.
27. The use of any of claims 24 to 26, wherein a first dose of the epigenetic factor is administered prior to the start of the administration of the CD33 targeting compound.

28. The use of claim 27, wherein the administration of the epigenetic factor is continued during the administration of the CD33 targeting compound.
29. The use of any of claim 24 to 28, wherein the bispecific construct is a bispecific antibody construct.
30. The use of claim 29, wherein the bispecific antibody construct is a bispecific single chain antibody construct.
31. The use of claim 29 or 30, wherein the bispecific antibody construct binds to human and cynomolgous CD3 and CD33.
32. The use of any of claim 29 to 31, wherein the bispecific antibody construct comprises
 - a first binding domain specifically binding to CD33 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 6, 24, 42, 60, 78, 96, 114 and 132 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 1, 19, 37, 55, 73, 91, 109 and 127; and
 - a second binding domain specifically binding to CD3 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 154, 157, 160, 163, 166, 169 and 172 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 155, 158, 161, 164, 167, 170 and 173.
33. The use of claim 32, wherein the bispecific antibody construct comprises an amino acid sequence as depicted in any of SEQ ID NOs: 13, 15, 17, 31, 33, 35, 49, 51, 53, 67, 69, 71, 85, 87, 89, 103, 105, 107, 121, 123, 125, 139, 141, 143, 148, 150, 152, 215, 217, 219, 221, 223, 225 and 227.
34. The use of any of claims 24 to 33, wherein the myeloid leukemia is selected from the group consisting of acute myeloblastic leukemia, chronic neutrophilic leukemia, myeloid dendritic cell leukemia, accelerated phase chronic myelogenous leukemia, acute myelomonocytic leukemia, juvenile myelomonocytic leukemia, chronic myelomonocytic leukemia, acute basophilic leukemia, acute eosinophilic leukemia, chronic eosinophilic leukemia, Acute megakaryoblastic leukemia, essential thrombocytosis, acute erythroid leukemia, polycythemia vera, myelodysplastic syndrome, acute panmyelosis, myeloid sarcoma, and acute biphenotypic leukaemia.

35. A method for the treatment of a myeloid leukemia, the method comprising the administration of at least one epigenetic factor and a CD33 targeting compound to a patient in the need thereof, wherein
- (a) the CD33 targeting compound is a bispecific construct comprising a first binding domain specifically binding to CD33 and a second binding domain specifically binding to CD3; and
 - (b) the at least one epigenetic factor is selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors, hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone methyltransferase (HMT) inhibitors and ATRA (All Trans-retinoic acid).
36. The method of claim 35, wherein the at least one epigenetic factor is selected from the group comprising
- (a) a histone deacetylase (HDAC) inhibitor selected from the group consisting of panobinostat, vorinostat, romidepsin, N-acetyldinaline, belinostat, givinostat, entinostat, mocetinostat, EVP-0334, SRT501, CUDC-101, Quisinostat, abexinostat, LAQ824, and valproic acid;
 - (b) a DNA methyltransferase (DNMT) I inhibitor selected from the group consisting of 5-azacitidine, decitabine, hydralazine, zebularine, procainamide, (-)-epigallocatechin-3-gallate, MG98, RG108, and SGI-110; and
 - (c) a histone methyltransferase (HMT) inhibitor selected from the group consisting of LSD1 (KDM1A) demethylase inhibitor, and chaetocin.
37. The method of claim 35 or 36, wherein
- (a) the epigenetic factor is administered prior to the administration of the CD33 targeting compound;
 - (b) the epigenetic factor is administered subsequent to the administration of the CD33 targeting compound; or
 - (c) the epigenetic factor and the CD33 targeting compound are administered simultaneously.
38. The method of any of claims 35 to 37, wherein a first dose of the epigenetic factor is administered prior to the start of the administration of the CD33 targeting compound.
39. The method of claim 38, wherein the administration of the epigenetic factor is continued during the administration of the CD33 targeting compound.

40. The method of any of any of claims 35 to 39, wherein the bispecific construct is a bispecific antibody construct.
41. The method of claim 40, wherein the bispecific antibody construct is a bispecific single chain antibody construct.
42. The method of claim 40 or 41, wherein the bispecific antibody construct binds to human and cynomolgous CD3 and CD33.
43. The method of any of any of claims 40 to 42, wherein the bispecific antibody construct comprises
 - a first binding domain specifically binding to CD33 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 6, 24, 42, 60, 78, 96, 114 and 132 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 1, 19, 37, 55, 73, 91, 109 and 127; and
 - a second binding domain specifically binding to CD3 and comprising a VL chain having an amino acid sequence as depicted in SEQ ID NO: 154, 157, 160, 163, 166, 169 and 172 and a VH chain having an amino acid sequence as depicted in SEQ ID NO: 155, 158, 161, 164, 167, 170 and 173.
44. The method of claim 43, wherein the bispecific antibody construct comprises an amino acid sequence as depicted in any of SEQ ID NOs: 13, 15, 17, 31, 33, 35, 49, 51, 53, 67, 69, 71, 85, 87, 89, 103, 105, 107, 121, 123, 125, 139, 141, 143, 148, 150, 152, 215, 217, 219, 221, 223, 225 and 227.
45. The method of any of claims 35 to 44, wherein the myeloid leukemia is selected from the group consisting of acute myeloblastic leukemia, chronic neutrophilic leukemia, myeloid dendritic cell leukemia, accelerated phase chronic myelogenous leukemia, acute myelomonocytic leukemia, juvenile myelomonocytic leukemia, chronic myelomonocytic leukemia, acute basophilic leukemia, acute eosinophilic leukemia, chronic eosinophilic leukemia, Acute megakaryoblastic leukemia, essential thrombocytosis, acute erythroid leukemia, polycythemia vera, myelodysplastic syndrome, acute panmyelosis, myeloid sarcoma, and acute biphenotypic leukaemia.
46. A kit comprising a pharmaceutical composition of any of claims 1 to 12 or an epigenetic factor of any of claims 13 to 23 and a bispecific CD33 targeting compound comprising a first binding domain specifically binding to CD33 and a second binding

domain specifically binding to CD3, to be employed in the amelioration and/or treatment of a myeloid leukemia.