

An object of the present invention is to fulfill all or part of these needs.

Summary of invention

The present ~~invention~~disclosure relates to CD16+ cells, NK cells or NK cell precursors, in combination with a recombinant polypeptide; wherein said recombinant polypeptide comprises (i) a modified Fc region, preferably with at least one modification in a C_H2 domain, and (ii) a ligand binding domain, said modified Fc region being capable of binding to said cells or precursors thereof.

As specified in the examples hereinafter, the inventors have noted that CD16+ cells, in particular NK cells, in combination with a recombinant polypeptide capable of binding to a ligand or ligands, remain stable *in vitro* and *in vivo* for several days. Furthermore, it has been noted that these armed CD16+ cells, in particular NK cells, were thus capable of specifically targeting target cells through recognition of the appropriate ligand(s).

The CD16 cell surface marker is also referred herein as the FCγRIII surface receptor.

According to one of its objects, the present ~~invention~~disclosure relates to a pharmaceutical composition comprising a CD16+ cell, in combination with a recombinant polypeptide; wherein said recombinant polypeptide comprises (i) a modified Fc (fragment crystallizable) region, and (ii) a ligand binding domain, said Fc region being capable of binding to said CD16+ cell.

According to one of its objects, the present ~~invention~~disclosure also relates to a pharmaceutical composition comprising a NK (Natural Killer) cell or a NK cell precursor, in combination with a recombinant polypeptide; wherein said recombinant polypeptide comprises (i) a modified Fc (fragment crystallizable) region, and (ii) a ligand binding domain, said Fc region being capable of binding to said NK cell or to the NK cell precursor.

The inventors have unexpectedly noted that a NK cell, which is a CD16+ cell, taken from an individual and armed *in vitro* with a recombinant polypeptide as defined in the present ~~invention~~disclosure, allows increasing NK cell cytotoxicity against target cell. Surprisingly, and contrary to the teachings of Moore *et al.* 2010, the binding between the Fc receptor of an NK cell and a recombinant polypeptide according to the ~~invention~~disclosure remains stable and specific for several days, particularly for at least 7 days, *in vitro* and *in vivo*. Therefore, this combination of an NK cell and a recombinant polypeptide as defined in the present description, which will be referred to as “armed NK cell”, proves to be an effective therapeutic solution against any disease the treatment of which implies the destruction of target cells of interest. This therapeutic solution does not need a genetic modification of the NK cell, unlike NK-CAR cells specifically described in the review of Wang *et al.* (Luyao Wang, Mei Dou, Qingxia Ma, Ruixue Yao, Jia Liu; Chimeric antigen receptor (CAR)-modified NK cells against cancer: Opportunities and challenges; International Immunopharmacology 74 (2019) 105695), which makes this combination much simpler to use than NK-CAR cells. In fact, a single sample of NK cells, for example taken from cord blood, is sufficient to treat any individual for any and all targeting specificities for which an appropriate ligand can be identified.

The inventors thus provide experimental evidence that CD16+ cells, which may in particular correspond to the Natural Killer cell lineage, can be combined efficiently and in a stable manner with a recombinant polypeptide comprising a modified Fc region.

Further, it has been demonstrated on the present ~~invention~~disclosure that a recombinant polypeptide as disclosed herein has a high affinity for the CD16 receptor, in particular the CD16a receptor, for a

long period of time.

The inventors also provide experimental evidence that the attachment to the recited cells is also stable, and even suitable in therapy, when the recombinant polypeptide is bound non-covalently. Accordingly, “binding” or “attachment” of the recited recombinant polypeptide to a CD16+ cell and/or NK cell or NK precursor is preferably considered as “non-covalent”.

The inventors also propose that the corresponding strategy is suitable for administering therapeutic compounds with decreased doses and/or reduced side-effects.

The inventors also propose that the corresponding strategy is suitable for binding, in particular non-covalent binding, of such CD16+ cells and/or NK cells and/or precursors thereof with a plurality of recombinant polypeptides with a modified Fc region, in the sense of the ~~invention~~disclosure.

According to one aspect, the disclosure relates to a composition comprising a CD16+ cell or a NK (Natural Killer) cell in combination with a recombinant polypeptide capable of binding to the FcγRIII (CD16) surface protein, wherein the recombinant polypeptide is non-covalently bound to the FcγRIII (CD16) surface protein expressed by the CD16+ cell or the NK (Natural Killer) cell, and wherein said recombinant polypeptide comprises:

- (i) a modified C_H2 domain of a wild-type human IgG1, bound, optionally through a linker, to
- (ii) a ligand binding domain,

wherein the ligand binding domain comprises a sequence capable of binding to a target ligand; wherein the modified C_H2 domain is characterized by comprising mutations S239D and I332E with respect to the C_H2 domain of a wild-type human IgG1, and wherein said C_H2 domain of a wild-type human IgG1 is represented by SEQ ID NO 1, or by a sequence with a percentage of identity of at least 85% with the amino acid sequence SEQ ID NO. 1, and comprises sequence positions 231-340, according to the EU numbering.

According to one of these objects, the ~~invention~~disclosure relates to a composition comprising a CD16+ cell in combination with a recombinant polypeptide capable of binding to the FcγRIII (CD16) surface protein, preferably to the FcγRIIIa/CD16a surface protein, wherein the recombinant polypeptide is non-covalently bound to the FcγRIII (CD16) surface protein, preferably to the FcγRIIIa/CD16a surface protein, expressed by the CD16+ cell, and wherein said recombinant polypeptide comprises:

- (i) a modified C_H2 domain of a wild-type human IgG1, bound, optionally through a linker, to
- (ii) a ligand binding domain,

wherein the ligand binding domain comprises a sequence capable of binding to a target ligand; wherein the modified C_H2 domain is characterized by comprising mutations S239D and I332E with respect to the C_H2 domain of a wild-type human IgG1, and wherein said C_H2 domain of a wild-type human IgG1 is represented by SEQ ID NO 1, or by a sequence with a percentage of identity of at least 85% with amino acid sequence SEQ ID NO. 1, and comprises sequence positions 231-340, according to the EU numbering.

According to some ~~embodiment~~examples, the C_H2 domain of a wild-type human IgG1 is represented by SEQ ID NO. 1. Hence, according to some ~~embodiment~~examples, the modified C_H2 domain is modified with respect to the C_H2 domain of the wild-type human IgG1 represented by SEQ ID NO 1

According to some ~~embodiment~~examples, the FcγRIII (CD16) surface protein is FcγRIIIa/CD16a surface protein.

According to some ~~embodiment~~examples, the modified C_H2 domain comprises at least one additional mutation selected from the list consisting of H268F, S324T, G236A and A330L with respect to the C_H2 domain of a wild-type human IgG1.

According to some ~~embodiment~~examples, the modified C_H2 domain comprises at least one additional mutation selected from the list consisting of H268F, S324T and A330L with respect to the C_H2 domain of a wild-type human IgG1.

According to some ~~embodiment~~examples, the modified C_H2 domain comprises at least one additional mutation selected from the list consisting of H268F and S324T with respect to the C_H2 domain of a wild-type human IgG1.

According to some ~~embodiment~~examples, the modified C_H2 domain comprises amino acid substitutions S239D, I332E and S324T, according to EU numbering, with respect to the C_H2 domain of a wild-type human IgG1.

According to some [embodimentexamples](#), the modified C_H2 domain comprises amino acid substitutions S239D, I332E and H268F, according to EU numbering, with respect to the C_H2 domain of a wild-type human IgG1.

According to some [embodimentexamples](#), the modified C_H2 domain comprises amino acid substitutions S239D, I332E and A330L, according to EU numbering, with respect to the C_H2 domain of a wild-type human IgG1.

According to some [embodimentexamples](#), the modified C_H2 domain comprises amino acid substitutions S239D, I332E, H268F and S324T, according to EU numbering, with respect to the C_H2 domain of a wild-type human IgG1.

According to some [embodimentexamples](#), the modification of the C_H2 domain with respect to the C_H2 domain of a wild-type human IgG1 consists of mutations S239D and I332E.

According to some [embodimentexamples](#), the CD16+ cell is allogeneic with respect to an individual in need thereof.

According to some [embodimentexample](#), the recombinant polypeptide is an antibody and the modification in the C_H2 domain is symmetrical, or asymmetrical, with respect to the pair of C_H2 domains (or the pair of heavy chains) constituting the antibody.

According to some [embodimentexamples](#), the recombinant polypeptide comprises a human IgG1 Fc (fragment crystallizable) region comprising the modified C_H2 domain.

According to some [embodimentexamples](#), the recombinant polypeptide is an antibody or a fragment thereof comprising the modified CH2 domain as defined herein or the Fc region as defined herein and a ligand binding domain selected from the ligand binding domain of any of the following antibodies: Abagovomab, Abatacept, Abciximab, Abituzumab, Abrilumab, Actoxumab, Adalimumab, Adecatumab, Aducanumab, Aflibercept, Afutuzumab, Alacizumab, Alefacept, Alemtuzumab, Alirocumab, Altumomab, Amatixumab, Anatomomab, Anetumab, Anifromumab, Anrukinzumab, Apolizumab, Arcitumomab, Ascrinvacumab, Aselizumab, Atezolizumab, Atinumab, Altizumab, Atorolimumab, Bapineuzumab, Basiliximab, Bavituximab, Bectumomab, Begelomab, Belatacept, Belimumab, Benralizumab, Bertilimumab, Besilesomab, Bevacizumab, Bezlotoxumab, Biciromab, Bimagrumab, Bimekizumab, Bivatuzumab, Blinatumomab, Blosozumab, Bococizumab, Brentuximab, Briakimumab, Brodalumab, Brolocizumab, Bronticizumab, Canakinumab, Cantuzumab, Caplacizumab, Capromab, Carlumab, Catumaxomab, Cedelizumab, Certolizumab, Cetixumab, Citatuzumab, Cixutumumab, Clazakizumab, Clenoliximab, Clivatuzumab, Codrituzumab, Coltuximab, Conatumumab, Concizumab, Crenezumab, Dacetuzumab, Daclizumab, Dalotuzumab, Dapirolizumab, Daratumumab, Dectrekumab, Demcizumab, Denintuzumab, Denosumab, Derlotixumab, Detumomab, Dinutuximab, Diridavumab, Dorlinomab, Drozitumab, Dupilumab, Durvalumab, Dusigitumab, Echromeximab, Eculizumab, Edobacomab, Edrecolomab, Efalizumab, Efungumab, Eldelumab, Elgemtumab, Elotuzumab, Elsilimomab, Emactuzumab, Emibetuzumab, Enavatuzumab, Enfortumab, Enlimomab, Enoblituzumab, Enokizumab, Enoticumab, Ensituximab, Epitumomab, Epratuzomab, Erlizumab, Ertumaxomab, Etanercept, Etaracizumab, Etrolizumab, Evinacumab, Evolocumab, Exbivirumab, Fanolesomab, Faralimomab, Farletuzumab, Fasimumab, Felvizumab, Fezкимumab, Ficlatuzumab, Figitumumab, Firivumab, Flanvotumab, Fletikumab, Fontolizumab, Foralumab, Foravirumab, Fresolimumab, Fulramumab, Futuximab, Galiximab, Ganitumab, Gantenerumab, Gavilimumab, Gemtuzumab, Gevokizumab, Girentuximab, Glembatumumab, Golimumab, Gomiliximab, Guselkumab, Ibalizumab, Ibritumomab,

Icrucumab, Idarucizumab, Igovomab, Imalumab, Imciromab, Imgatuzumab, Inclacumab, Indatuximab, Indusatumab, Infliximab, Intetumumab, Inolimomab, Inotuzumab, Ipilimumab, Iratumumab, Isatuximab, Itolizumab, Ixekizumab, Keliximab, Labetuzumab, Lambrolizumab, Lampalizumab, Lebrikizumab, Lemalesomab, Lenzilumab, Lerdelimumab, Lexatumumab, Libivirumab, Lifestuzumab, Ligelizumab, Lilotomab, Lintuzumab, Lirilumab, Lodelcizumab, Lokivetmab, Lorvotuzumab, Lucatumumab, Lulizumab, Lumiliximab, Lumretuzumab, Mapatumumab, Margetuximab, Maslimomab, Mavrilimumab, Matuzumab, Mepolizumab, Metelimumab, Milatuzumab, Minetumomab, Mirvetuximab, Mitumomab, Mogamulizumab, Morolimumab, Motavizumab, Moxetumomab, Muromonab-CD3, Nacolomab, Namilumab, Naptumomab, Narnatumab, Natalizumab, Nebacumab, Necitumumab, Nemolizumab, Nerelimomab, Nesvacumab, Nimotuzumab, Nivolumab, Nofetumomab, Obiltoxaximab, Obinutuzumab, Ocaratuzumab, Ocrelizumab, Odulimomab, Ofatumumab, Olaratumab, Olokizumab, Omalizumab, Onartuzumab, Ontuxizumab, Opicinumab, Oportuzumab, Oregovomab, Orticumab, Otelixizumab, Oltertuzumab, Oxelumab, Ozanezumab, Ozoralizumab, Pagibaximab, Palivizumab, Panitumumab, Pankomab, Panobacumab, Parsatuzumab, Pascolizumab, Pasotuxizumab, Pateclizumab, Patritumab, Pembrolizumab, Pemtumomab, Perakizumab, Pertuzumab, Pexelizumab, Pidilizumab, Pinatuzumab, Pintumomab, Polatuzumab, Ponezumab, Priliximab, Pritumumab, Quilizumab, Racotumomab, Radretumab, Rafivirumab, Ralpancizumab, Ramucirumab, Ranibizumab, Raxibacumab, Refanezumab, Regavirumab, Reslizumab, Rilonacept, Rilotumumab, Rinucumab, Rituximab, Robatumumab, Roledumab, Romosozumab, Rontalizumab, Rovelizumab, Ruplizumab, Sacituzumab, Samalizumab, Sarilumab, Satumomab, Secukimumab, Seribantumab, Setoxaximab, Sevirumab, Sibrotuzumab, Sifalimumab, Siltuximab, Siplizumab, Sirukumab, Sofituzumab, Solanezumab, Solitumab, Sonepcizumab, Sontuzumab, Stamulumab, Sulesomab, Suvizumab, Tabalumab, Tacatuzumab, Tadocizumab, Talizumab, Tanezumab, Taplitumomab, Tarextumab, Tefibazumab, Telimomab aritox, Tenatumomab, Teneliximab, Teplizumab, Tesidolumab, TGN 1412, Ticlimumab, Tildrakizumab, Tigatuzumab, TNX-650, Tocilizumab, Toralizumab, Tosatoxumab, Tositumomab, Tovetumab, Tralokimumab, Trastuzumab, TRBS07, Tregalizumab, Tremelimumab, Trevogrumab, Tucotuzumab, Tuvirumab, Ublituximab, Ulocuplumab, Urelumab, Urtoxazumab, Ustekimumab, Vandortuzumab, Vantictumab, Vanucizumab, Vapaliximab, Varlimumab, Vatelizumab, Vedolizumab, Veltuzumab, Vepalimumab, Vesencumab, Visilizumab, Volocixumab, Vorsetuzumab, Votumumab, Zalutumimab, Zanolimumab, Zatuximab, Ziralimumab, Ziv-Aflibercept, and Zolimomab.

According to some embodiment examples, compositions as defined herein may be for use as a medicament.

According to some preferred embodiment examples, compositions as defined herein may be for use in a method for treating or preventing a cancer, an autoimmune disease, or an infectious disease in an individual in need thereof.

According to one aspect, the disclosure relates to use of the composition as defined herein as a medicament, preferably for use in a method for treating or preventing a cancer, an autoimmune disease, or an infectious disease in an individual in need thereof.

According to another ~~of these objects aspect~~, the invention disclosure also relates to a pharmaceutical composition comprising the composition as defined herein, optionally further comprising an excipient or a pharmacologically acceptable vehicle.

According to some embodiment examples, the CD16+ cell is allogeneic with respect to an individual in need thereof may be for use as a medicament.

According to some preferred embodiment example, a pharmaceutical composition as defined herein may be for use in a method for treating or preventing a cancer, an autoimmune disease, or an infectious disease in an individual in need thereof.

According to yet another aspect, the disclosure relates to use of the composition as defined herein or a pharmaceutical composition as defined herein, wherein the CD16+ cell or the NK (Natural Killer) cell is allogeneic with respect to an individual in need thereof, as a medicament, preferably for use in a method for treating or preventing a cancer, an autoimmune disease, or an infectious disease in an individual in need thereof.

According to another of these objects, the invention disclosure also relates to a composition comprising a NK

(Natural Killer) cell in combination with a recombinant polypeptide capable of binding to the FcγRIII (CD16) surface protein, wherein the recombinant polypeptide is non-covalently bound to the FcγRIII (CD16) surface protein expressed by the NK (Natural Killer) cell, and wherein said recombinant polypeptide comprises:

- (i) a modified C_H2 domain of a wild-type human IgG1, bound, optionally through a linker, to
- (ii) a ligand binding domain,

wherein the ligand binding domain comprises a sequence capable of binding to a target ligand; wherein the modified C_H2 domain is characterized by comprising mutations S239D and I332E with respect to the C_H2 domain of a wild-type human IgG1, and wherein said C_H2 domain of a wild-type human IgG1 is represented by SEQ ID NO. 1, or by a sequence with a percentage of identity of at least 85% with the amino acid sequence SEQ ID NO. 1, and comprises sequence positions 231-340, according to the EU numbering.

According to some ~~embodiment~~examples, the CD16 cell is allogeneic with respect to an individual in need thereof.

According to some ~~embodiment~~examples, the recombinant polypeptide is an antibody and the modification in the C_H2 domain is symmetrical, or asymmetrical, with respect to the pair of C_H2 domains (or the pair of heavy chains) constituting the antibody.

According to some ~~embodiment~~examples, the recombinant polypeptide comprises a human IgG1 Fc (fragment crystallizable) region comprising the modified C_H2 domain.

According to some ~~embodiment~~examples, the recombinant polypeptide is an antibody or a fragment thereof comprising the C_H2 domain as defined herein, and a ligand binding domain selected from the ligand binding domain of any of the antibodies as defined herein.

According to another of these objects, the ~~invention~~disclosure also relates to a pharmaceutical composition comprising an NK (Natural Killer) cell, in combination with a recombinant polypeptide; wherein said recombinant polypeptide comprises (i) a modified Fc (fragment crystallizable) region, and (ii) a ligand binding domain, said Fc region being capable of binding to said NK cell and comprising at least one modified C_H2 domain of a wild-type human IgG1, wherein the modified C_H2 domain is characterized by comprising mutations S239D and I332E with respect to the C_H2 domain of a wild-type human IgG1, and wherein said C_H2 domain of a wild-type human IgG1 is represented by SEQ ID NO 1, or by a sequence with a percentage of identity of at least 85% with the amino acid sequence SEQ ID NO. 1, and comprises sequence positions 231-340, according to the EU numbering.

According to another ~~of these objects~~aspect, the ~~invention~~disclosure also relates to a NK cell allogeneic with respect to an individual in need thereof attached to a recombinant polypeptide, wherein said recombinant polypeptide comprises (i) a modified Fc (fragment crystallizable) region, and (ii) a binding domain, said Fc region being capable of binding to said NK cell and comprising at least one modified C_H2 domain of a wild-type human IgG1 as defined herein; for use as a medicament.

According to yet another aspect, the disclosure relates to a kit comprising:
- a first part comprising a CD16+ cell or a NK cell, preferably a CD16+ cell or a NK cell allogeneic with respect to an individual in need thereof; and
- a second part comprising a recombinant polypeptide as defined herein; for use as a medicament.

According to another of these objects, the ~~invention~~disclosure also relates to a kit comprising:
 - a first part comprising a CD16+ cell, preferably a CD16+ cell allogeneic with respect to an individual in need thereof; and
 - a second part comprising a recombinant polypeptide as defined herein; for use as a medicament.

According to another of these objects, the ~~invention~~disclosure also relates to a kit comprising:

- a first part comprising a NK cell, preferably a NK cell allogeneic with respect to an individual in need thereof; and

5 - a second part comprising a recombinant polypeptide as defined herein; for use as a medicament.

According to another of these objects, the ~~invention~~disclosure also relates to a kit comprising:

- a first part including a NK cell, preferably a NK cell allogeneic with respect to an individual in need thereof; and

10 - a second part including a recombinant polypeptide comprising (i) a modified Fc (fragment crystallizable) region, and (ii) a ligand binding domain; said Fc region being capable of binding to said NK cell and comprising at least one modified C_H2 domain of a wild-type human IgG1 as defined herein; for use as a medicament.

15 According to another of these objects, the ~~invention~~disclosure also relates to a pharmaceutical composition comprising a CD16+ cell, in combination with a recombinant polypeptide; wherein said recombinant polypeptide comprises (i) a modified Fc (fragment crystallizable) region on the amino acid sequence of the Fc region, and (ii) a ligand binding domain, said Fc region being capable of binding to said CD16+ cell, and further comprising an excipient or a pharmacologically acceptable vehicle.

20 According to another of these objects, the ~~invention~~disclosure also relates to a pharmaceutical composition comprising a NK (Natural Killer) cell or a NK cell precursor, in combination with a recombinant polypeptide; wherein said recombinant polypeptide comprises (i) a modified Fc (fragment crystallizable) region on the amino acid sequence of the Fc region, and (ii) a ligand binding domain, said Fc region being capable of binding to said NK cell or precursor thereof, and further comprising an excipient or a pharmacologically acceptable vehicle.

30 According to another one of these objects, the ~~invention~~disclosure also relates to a NK cell allogeneic or autologous with respect to an individual in need thereof, or a NK cell precursor attached to a recombinant polypeptide, wherein said recombinant polypeptide comprises (i) a modified Fc region, capable of binding to said NK cell or precursor thereof, and (ii) a ligand binding domain; for use as a medicament.

35 According to another one of these objects, the ~~invention~~disclosure relates to a kit comprising:

- a first part including a NK cell, preferably allogeneic or autologous with respect to an individual in need thereof, or a NK cell precursor;

40 - a second part including a recombinant polypeptide comprising (i) a modified Fc region and (ii) a ligand binding domain; said Fc region being capable of binding to said NK cell or to a NK cell precursor; for use as a medicament.

45 According to another one of these objects, the ~~invention~~disclosure also relates to the use of the pharmaceutical composition according to the ~~invention~~disclosure, for use as a medicament.

50 According to another one of these objects, the ~~invention~~disclosure also relates to the use of the pharmaceutical composition, the NK cell allogeneic or autologous with respect to an individual in need thereof, or NK cell precursor or the kit according to the ~~invention~~disclosure, in a method for treating or preventing a disease wherein it is beneficial to bring said allogeneic or autologous NK cell or NK cell precursor close to a target cell in order to destroy said target cell.

According to another one of these objects, the ~~invention~~disclosure also relates to the use of the pharmaceutical

composition, the NK cell allogeneic or autologous with respect to an individual in need thereof, or NK cell precursor or the kit according to the invention disclosure, in a method for treating or preventing a cancer, an autoimmune disease and derivatives thereof or an infectious disease in an individual in need thereof.

5 According to another one of these objects, the invention disclosure relates to an *in vitro* or *ex vivo* method for preparing a pharmaceutical composition comprising a NK cell or a NK cell precursor, comprising the following steps: a) providing a NK cell, preferably allogeneic or autologous with respect to an individual in need thereof, or a NK cell precursor; b) contacting said NK cell or said
10 NK cell precursor with a recombinant polypeptide, wherein said recombinant polypeptide comprises (i) a modified Fc region, and (ii) a ligand binding domain, said Fc region being capable of binding to said NK cell or to a NK cell precursor.

15 According to one embodiment example, the pharmaceutical composition comprising a NK cell or a NK cell precursor, in combination with a recombinant polypeptide; wherein said recombinant polypeptide comprises (i) a modified Fc (fragment crystallizable) region, and (ii) a ligand binding domain, said Fc region being capable of binding to said NK cell or precursor thereof, can further comprise an excipient or a pharmacologically acceptable vehicle.

20 According to one embodiment example, the modified Fc region can comprise an amino acid sequence of any one of SEQ ID NO. 2 to 13.

25 According to one embodiment example, the modified Fc region can comprise an amino acid sequence having a sequence identity of at least 70% with the amino acid sequence SEQ ID NO. 2, particularly a sequence identity of at least 80% with the amino acid sequence SEQ ID NO. 2, particularly a sequence identity of at least 90% with the amino acid sequence SEQ ID NO. 2, and preferably the modified Fc region comprises an amino acid sequence having 100% identity with SEQ ID NO. 2.

30 According to one embodiment example, the modified Fc region of the recombinant polypeptide can comprise at least one modified C_H2 domain.

35 According to a particular embodiment example, the modified C_H2 domain of the Fc region of the recombinant polypeptide can comprise an amino acid sequence of any one of SEQ ID NO. 2 to 13 or an amino acid sequence having a sequence identity of at least 70% with the amino acid sequence SEQ ID NO. 2, particularly a sequence identity of at least 80% with the amino acid sequence SEQ ID NO. 2, particularly a sequence identity of at least 90% with the amino acid sequence SEQ ID NO. 2, and preferably the modified C_H2 domain comprises an amino acid sequence having 100% identity with SEQ ID NO. 2.

40 According to one embodiment example, the CD16⁺ cell and/or the NK cell can be allogeneic with respect to an individual in need thereof.

45 **Brief description of drawings**

Figure 1 represents the binding specificity of the Fc SDH, Fc LALA and Fc WT polypeptides and antibodies in combination with CD45⁺/CD56⁺/CD3⁻ eNK cells (*in vitro* NK cells from cord blood),

50 Figure 2 represents the binding stability between the Fc SDH, Fc LALA and Fc WT polypeptides with the Fc receptor (CD16A) of CD16⁺/CD56⁺/CD45⁺/CD3⁻ eNK cells,