The present disclosure also provides a method of determining a subject's suitability for entry into a drug screening trial, comprising performing the method of the invention and identifying the subject as being more suitable for entry into a drug screening trial if the subject has a lower level of soluble CD52 glycoprotein, a lower frequency of $CD52^{hi}$ cells, or a reduced activity of $CD52^{hi}$ cells than the reference sample. For example, the drug screening trial is an anti-diabetic drug screening trial.

In addition, the present disclosure also provides a method of identifying an agent capable of mimicking the effector T-cell-suppressing, and/or immune response suppressing, function of a soluble CD52 glycoprotein, the method comprising determining whether a test agent suppresses effector T-cell function and/or an immune response.

The present disclosure also provides a method of identifying a potential therapeutic agent for the treatment or prevention of a disease or condition mediated by effector T-cell function, inflammation or sepsis, the method comprising contacting a test agent with a $CD52^{hi}$ cell or $CD52^{hi}$ cell population, and detecting any one or more of the level of soluble CD52 glycoprotein produced by the cell or cell population, the frequency of $CD52^{hi}$ cells and/or the activity of $CD52^{hi}$ cells, and identifying the test agent as a potential therapeutic agent for the treatment or prevention of a disease or condition mediated by effector T-cell function, inflammation or sepsis, if the level of soluble CD52 glycoprotein, the frequency of $CD52^{hi}$ cells and/or the activity of $CD52^{hi}$ cells is increased after contact with the test agent.

The present disclosure also provides any one or more of:

i) a soluble CD52 glycoprotein,

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein;

iii) a polynucleotide encoding the peptide portion of soluble CD52 glycoprotein of part i) or the fusion protein of part ii);

iv) a vector comprising the polynucleotide of part iii);

v) an isolated cell comprising the polynucleotide of part iii) or the vector of part iv);

vi) cell culture medium, or a fraction thereof comprising soluble CD52 glycoprotein, isolated from a cell culture comprising the cell of part v); and

vii) a pharmaceutical composition comprising any one or more of i) to vi) and a pharmaceutically acceptable carrier,

for use in treating or preventing sepsis or multiple sclerosis.

The present disclosure also provides the use of any one or more of:

i) a soluble CD52 glycoprotein,

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein;

iii) a polynucleotide encoding the peptide portion of soluble CD52 glycoprotein of part i) or the fusion protein of part ii);

iv) a vector comprising the polynucleotide of part iii);

v) an isolated cell comprising the polynucleotide of part iii) or the vector of part iv);

vi) cell culture medium, or a fraction thereof comprising soluble CD52 glycoprotein, isolated from a cell culture comprising the cell of part v); and

vii) a pharmaceutical composition comprising any one or more of i) to vi) and a pharmaceutically acceptable carrier,

in the manufacture of a medicament for the treatment or prevention of sepsis or multiple sclerosis.

The present disclosure also provides a method of diagnosing a subject's susceptibility to developing sepsis or multiple sclerosis, the method comprising:

detecting the level of soluble CD52 glycoprotein in a sample taken from the subject; and

comparing the level of soluble CD52 glycoprotein detected in the sample taken from the subject with a reference level determined from one or more healthy subjects,

wherein a lower level of soluble CD52 glycoprotein detected in the sample taken from the subject compared to the reference level indicates that the subject has an increased susceptibility to developing sepsis or multiple sclerosis.

The present disclosure also provides a method of diagnosing a subject's susceptibility to developing sepsis, the method comprising:

detecting the frequency of $CD52^{hi}$ cells in a sample taken from a subject; and

comparing the frequency of $CD52^{hi}$ cells detected in the sample taken from the subject with a reference level determined from one or more healthy subjects,

wherein a lower frequency of $CD52^{hi}$ cells detected in the sample taken from the subject compared to the reference level indicates that the subject has an increased susceptibility to developing sepsis.

The present disclosure also provides a method of diagnosing a subject's susceptibility to developing sepsis, the method comprising:

detecting the activity of $CD52^{hi}$ cells in a sample taken from a subject; and

comparing the activity of $CD52^{hi}$ cells detected in the sample taken from the subject with a reference level determined from one or more healthy subjects,

wherein a reduced activity of $CD52^{hi}$ cells detected in the sample taken from the subject compared to the reference level indicates that the subject has an increased susceptibility to developing sepsis.

The present disclosure also provides a method of identifying a potential therapeutic agent for the treatment or prevention of sepsis, the method comprising contacting a test agent with a $CD52^{hi}$ cell or $CD52^{hi}$ cell population, and detecting any one or more of the level of soluble CD52 glycoprotein produced by the cell or cell population, the frequency of $CD52^{hi}$ cells and/or the activity of $CD52^{hi}$ cells, and identifying the test agent as a potential therapeutic agent for the treatment or prevention of sepsis, if the level of soluble CD52 glycoprotein, the frequency of $CD52^{hi}$ cells and/or the activity of $CD52^{hi}$ cells is increased after contact with the test agent.

The features of any embodiment described herein shall be taken to apply mutatis mutandis to any other embodiment unless specifically stated otherwise.

The present disclosure is not to be limited in scope by the specific embodiments described herein, which are intended for the purpose of exemplification only. Functionally-equivalent products, compositions and methods are clearly within the scope of the invention, as described herein.

Throughout this specification, unless specifically stated otherwise or the context requires otherwise, reference to a single step, composition of matter, group of steps or group of compositions of matter shall be taken to encompass one and a plurality (i.e. one or more) of those steps, compositions of matter, groups of steps or group of compositions of matter.

The invention is hereinafter described by way of the following non-limiting Examples and with reference to the accompanying figures.

BRIEF DESCRIPTION OF THE ACCOMPANYING DRAWINGS

CLAIMS

1. Any one or more of:

i) a soluble CD52 glycoprotein;

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein;

iii) a polynucleotide encoding the peptide portion of soluble CD52 glycoprotein of part i) or the fusion protein of part ii);

iv) a vector comprising the polynucleotide of part iii);

v) an isolated cell comprising the polynucleotide of part iii) or the vector of part iv);

~~vi) an isolated $CD52^{hi}$ cell capable of producing soluble CD52 glycoprotein;~~

~~vii) an isolated cell population comprising a plurality of $CD52^{hi}$ cells capable of producing soluble CD52 glycoprotein;~~

~~viii)~~vi) cell culture medium, or a fraction thereof comprising soluble CD52 glycoprotein, isolated from a cell culture comprising the cell of part ~~vi~~v) ~~or the cell population of part vii)~~; and

~~ix) an agent capable of increasing the level of expression of soluble CD52 glycoprotein by a cell; and~~

~~x)~~vii) a pharmaceutical composition comprising any one or more of i) to ~~vii~~ix) and a pharmaceutically acceptable carrier,

for use in treating or preventing sepsis or multiple sclerosis.

2. The use of any one or more of:

i) a soluble CD52 glycoprotein,

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein;

iii) a polynucleotide encoding the peptide portion of soluble CD52 glycoprotein of part i) or the fusion protein of part ii);

iv) a vector comprising the polynucleotide of part iii);

v) an isolated cell comprising the polynucleotide of part iii) or the vector of part iv);

~~vi) an isolated CD52^{hi} cell capable of producing soluble CD52 glycoprotein;~~

~~vii) an isolated cell population comprising a plurality of CD52^{hi} cells capable of producing soluble CD52 glycoprotein;~~

~~viii)~~vi) cell culture medium, or a fraction thereof comprising soluble CD52 glycoprotein, isolated from a cell culture comprising the cell of part v~~i~~) ~~or the cell population of part vii)~~; and

~~ix) an agent capable of increasing the level of expression of soluble CD52 glycoprotein by a cell; and~~

~~x)~~vii) a pharmaceutical composition comprising any one or more of i) to ~~ix~~vi) and a pharmaceutically acceptable carrier,

in the manufacture of a medicament for the treatment or prevention of sepsis or multiple sclerosis.

3. The ~~soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, CD52^{hi} cell, cell population, cell culture medium, agent or pharmaceutical composition of claim 1, or the~~ use of claim 2, wherein the soluble CD52 glycoprotein comprises an amino acid sequence at least 60% identical to the amino acid sequence of any one or more of GQNDTSQTSSPS (SEQ ID NO: 3), SQNATSQSSPS (SEQ ID NO: 4), GQATTAASGTNKNSTSTKKTPLKS (SEQ ID

NO: 5), GQNSTAVTTPANKAATTAAATTKAAATTATKTTTAVRKTPGKPPKA (SEQ ID NO: 6) or GNSTTPRMTTKKVKSATPA (SEQ ID NO:7) and a carbohydrate.

4. The ~~soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, CD52^{hi} cell, cell population, cell culture medium, agent or pharmaceutical composition of claim 1 or claim 3, or the~~ use of claim 2 or claim 3, wherein the glycoprotein comprises an amino acid sequence which is at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% identical, or is 100% identical, to any one or more of the amino acid sequences identified in SEQ ID NOs: 3, 4, 5, 6 or 7.

5. The ~~soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, CD52^{hi} cell, cell population, cell culture medium, agent or pharmaceutical composition of any one of claims 1 and 3-4, or the~~ use of any one of claims 2-4, wherein any one or more of the soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, CD52^{hi} cell, cell population, cell culture medium, agent and pharmaceutical composition is present in an amount sufficient to suppress sepsis and/or multiple sclerosis or to reduce or eliminate at least one symptom thereof.

6. The ~~soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, CD52^{hi} cell, cell population, cell culture medium, agent or pharmaceutical composition of any one of claims 1 and 3-5, or the~~ use of any one of claims 2-5, wherein the carbohydrate portion of soluble CD52 glycoprotein is linked to one or more asparagine, serine, threonine, tyrosine, hydroxylysine, hydroxyproline, phosphoserine or tryptophan residues if present in the amino acid sequence.

7. The ~~soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, CD52^{hi} cell, cell population, cell culture medium, agent or pharmaceutical composition of any one of claims 1 and 3-6, or the~~ use of any one of claims 2-6, wherein the carbohydrate portion of soluble CD52 glycoprotein is linked to the asparagine (N) residue in SEQ ID NO: 3.

8. The ~~soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, CD52^{hi} cell, cell population, cell culture~~

~~medium, agent or pharmaceutical composition of any one of claims 1 and 3-7, or the~~ use of any one of claims 2-7, wherein the carbohydrate portion of soluble CD52 glycoprotein is any carbohydrate known to be attached to the extracellular portion of soluble CD52 glycoprotein in a host cell, such as a host lymphocyte or a host genital tract cell.

9. The ~~soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, CD52^{hi} cell, cell population, cell culture medium, agent or pharmaceutical composition of any one of claims 1 and 3-8, or the~~ use of any one of claims 2-8, wherein the carbohydrate portion of soluble CD52 glycoprotein comprises one or more bi-, tri- or tetra-antennary sugars, which may be terminally sialylated.

10. The ~~fusion protein, polynucleotide, vector, cell, CD52^{hi} cell, cell population, cell culture medium, agent or pharmaceutical composition of any one of claims 1 and 3-9, or the~~ use of any one of claims 2-9, wherein the fusion protein comprises a second protein which comprises an antibody fragment.

11. The ~~fusion protein, polynucleotide, vector, cell, CD52^{hi} cell, cell population, cell culture medium, agent or pharmaceutical composition of claim 10, or the~~ use of claim 10, wherein the antibody fragment is an Fc.

~~12. The soluble CD52 glycoprotein, fusion protein, cell culture medium, agent or pharmaceutical composition of any one of claims 1 and 3-11, wherein the soluble CD52 glycoprotein, fusion protein, cell culture medium, agent or composition is administered at a mucosal or transdermal site.~~

~~13~~12. The use of any one of claims 2-11, wherein the medicament is formulated for administration at a mucosal or transdermal site.

~~14~~13. A method of diagnosing a subject's susceptibility to developing sepsis or multiple sclerosis, the method comprising:

detecting the level of soluble CD52 glycoprotein in a sample taken from the subject; and

comparing the level of soluble CD52 glycoprotein detected in the sample taken from the subject with a reference level determined from one or more healthy subjects,
wherein a lower level of soluble CD52 glycoprotein detected in the sample taken from the subject compared to the reference level indicates that the subject has an increased susceptibility to developing sepsis or multiple sclerosis.

~~15~~14. A method of diagnosing a subject's susceptibility to developing sepsis ~~or multiple sclerosis~~, the method comprising:

detecting the frequency of $CD52^{hi}$ cells in a sample taken from a subject; and

comparing the frequency of $CD52^{hi}$ cells detected in the sample taken from the subject with a reference level determined from one or more healthy subjects,
wherein a lower frequency of $CD52^{hi}$ cells detected in the sample taken from the subject compared to the reference level indicates that the subject has an increased susceptibility to developing sepsis ~~or multiple sclerosis~~.

~~16~~15. A method of diagnosing a subject's susceptibility to developing sepsis ~~or multiple sclerosis~~, the method comprising:

detecting the activity of $CD52^{hi}$ cells in a sample taken from a subject; and

comparing the activity of $CD52^{hi}$ cells detected in the sample taken from the subject with a reference level determined from one or more healthy subjects,
wherein a reduced activity of $CD52^{hi}$ cells detected in the sample taken from the subject compared to the reference level indicates that the subject has an increased susceptibility to developing sepsis ~~or multiple sclerosis~~.

~~17~~16. The method of claim ~~15~~14, wherein the frequency of $CD52^{hi}$ cells is detected by detecting the level of membrane bound CD52 in the sample, by detecting the level of expression of CD52 protein in the sample, and/or by detecting the level of expression of CD52 mRNA in the sample.

~~18~~17. The method of any one of claims ~~14~~13-~~17~~16, wherein the sample is taken from a subject to which an antigen has been administered.

~~19~~18. The method of any one of claims ~~14~~13-~~18~~17, wherein the sample is taken from a local disease site in the subject.

~~20~~19. A method of identifying a potential therapeutic agent for the treatment or prevention of sepsis ~~or multiple sclerosis~~, the method comprising contacting a test agent with a $CD52^{hi}$ cell or $CD52^{hi}$ cell population, and detecting any one or more of the level of soluble CD52 glycoprotein produced by the cell or cell population, the frequency of $CD52^{hi}$ cells and/or the activity of $CD52^{hi}$ cells, and identifying the test agent as a potential therapeutic agent for the treatment or prevention of sepsis ~~or multiple sclerosis~~, if the level of soluble CD52 glycoprotein, the frequency of $CD52^{hi}$ cells and/or the activity of $CD52^{hi}$ cells is increased after contact with the test agent.