Herrath and Harrison, 2003). For example, in the nonobese diabetic (NOD) mouse model of type 1 diabetes (T1D) $CD4^+$ Treg cells induced by administered pancreatic islet autoantigens such as insulin (Bergerot *et al.*, 1994) or glutamic acid decarboxylase 65 (GAD65) (Tisch *et al.*, 1999), or transfer of $CD4^+$ Treg cells induced by proinsulin (Every *et al.*, 2006) or a putative pancreatic islet antigen (Tang *et al.*, 2004), have been shown to protect against autoimmune diabetes. However, in these models Treg cells have been studied in resting, polyspecific populations and not during the host's response to a particular antigen. Recently, proinsulin- and GAD65-specific human $CD4^+$ T-cell clones were generated and Treg clones were distinguished by their suppressor function *in vitro* (Dromey *et al.*, 2011). The cell surface membrane-anchored glycoprotein CD52 was shown to be upregulated in these expanded $CD4^+$ Treg clones. However, the mechanism of immune suppression has not previously been characterized.

SUMMARY OF THE INVENTION

The present inventors have identified a soluble mediator of Treg cell suppression. Accordingly, the present disclosure provides a pharmaceutical composition comprising any one or more of:

i) 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) cell culture medium, or a fraction thereof comprising soluble CD52 glycoprotein, isolated from a cell culture comprising the cell of part vi) 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 a pharmaceutically acceptable carrier.

In one aspect, there is provided a pharmaceutical composition comprising any one or more of:

i) soluble CD52 glycoprotein,

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein wherein the second protein comprises an antibody fragment and/or a purification tag;

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) cell culture medium, or a fraction thereof comprising soluble CD52 glycoprotein, isolated from a cell culture comprising the cell of part vi) 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 a pharmaceutically acceptable carrier.

In a preferred embodiment, 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. More preferably, 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.

In one example, the glycoprotein comprises an amino acid sequence at least 60% 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 the amino acid sequence of SEQ ID NO: 3, which represents the human soluble CD52 fragment.

Preferably, any one or more of the soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, cell population, cell culture medium and agent is present in an amount sufficient to suppress effector T-cell function and/or an immune response.

In a further embodiment, the soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, cell population, cell culture medium and agent is present in an amount sufficient such that the suppression of the immune response results in tolerance to at least one antigen such an autoantigen.

In another embodiment, any one or more of the soluble CD52 glycoprotein, fusion protein, cell, cell population, cell culture medium and agent is capable of suppressing effector T-cell function and/or is capable of reducing an immune response such as an immune response to an autoantigen.

In an embodiment, the composition comprises one or more of the soluble CD52 glycoprotein, fusion protein, cell culture medium or agent, and is formulated for mucosal and/or transdermal administration.

In a further embodiment, the composition further comprises insulin and/or an autoantigen.

The present disclosure also provides a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein.

In one aspect, there is provided a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein wherein the second protein comprises an antibody fragment and/or a purification tag.

Preferably, the soluble CD52 glycoprotein of the fusion protein comprises an amino acid sequence which is at least 60%, 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.

Preferably, the fusion protein is capable of suppressing effector T-cell function and/or is capable of reducing an immune response such as an immune response to an

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

x) the pharmaceutical composition of the invention,

to suppress effector T-cell function and/or to reduce an immune response, such as an immune response to an autoantigen.

In one aspect, there is provided a use of any one or more of:

i) soluble CD52 glycoprotein,

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein wherein the second protein comprises an antibody fragment and/or a purification tag;

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

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

x) the pharmaceutical composition as disclosed herein,

in the manufacture of a medicament for suppressing effector T-cell function and/or for reducing an immune response, such as an immune response to an autoantigen.

The present disclosure also provides a method of treating or preventing a disease or condition mediated by effector T-cell function, inflammation or sepsis, in a subject, the method comprising administering a therapeutically effective amount of any one or more of:

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

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

x) the pharmaceutical composition of the invention,

to the subject.

In an embodiment, the soluble CD52 glycoprotein, fusion protein, cell culture medium, agent or composition is administered at a mucosal or transdermal site.

The present disclosure also provides any one or more of:

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

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

x) the pharmaceutical composition of the invention,

for use in treating or preventing a disease or condition mediated by effector T-cell function, inflammation or sepsis.

In one aspect, there is provided any one or more of:

i) soluble CD52 glycoprotein,

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein wherein the second protein comprises an antibody fragment and/or a purification tag;

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

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

x) the pharmaceutical composition of any one of claims 1-~~1~~413,

for use in treating or preventing a disease or condition mediated by effector T-cell function, inflammation or sepsis.

Furthermore, the present disclosure provides for the use of any one or more of:

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

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

x) the pharmaceutical composition of the invention,

in the manufacture of a medicament for the treatment or prevention of a disease or condition mediated by effector T-cell function, inflammation or sepsis.

In one aspect, there is provided the use of any one or more of:

i) soluble CD52 glycoprotein,

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein wherein the second protein comprises an antibody fragment and/or a purification tag;

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

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

x) the pharmaceutical composition as disclosed herein,

in the manufacture of a medicament for the treatment or prevention of a disease or condition mediated by effector T-cell function, inflammation or sepsis.

In an embodiment, the medicament is formulated for administration at a mucosal or transdermal site.

In one example, the disease mediated by effector T-cell function is an autoimmune disease, such as type I diabetes or rheumatoid arthritis. In another

CLAIMS

1. A pharmaceutical composition comprising any one or more of:
   i) soluble CD52 glycoprotein,
   ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein wherein the second protein comprises an antibody fragment and/or a purification tag;
   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) cell culture medium, or a fraction thereof comprising soluble CD52 glycoprotein, isolated from a cell culture comprising the cell of part vi) 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 a pharmaceutically acceptable carrier.

~~2. The pharmaceutical composition of claim 1, 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.~~

~~3~~2. The pharmaceutical composition of claim 1, wherein the soluble CD52 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.

~~4~~3. The pharmaceutical composition of ~~any preceding~~ claim 1 or 2, wherein any one or more of the soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, cell population, cell culture medium and agent is present in an amount sufficient to suppress effector T-cell function and/or an immune response.

~~5~~4. The pharmaceutical composition of any preceding claim, 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.

~~6~~5. The pharmaceutical composition of any preceding claim, wherein the carbohydrate portion of soluble CD52 glycoprotein is linked to the asparagine (N) residue in SEQ ID NO: 3.

~~7~~6. The pharmaceutical composition of any preceding claim, 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.

~~8~~7. The pharmaceutical composition of any preceding claim, wherein the carbohydrate portion of soluble CD52 glycoprotein comprises one or more bi-, tri- or tetra-antennary sugars, which may be terminally sialylated.

~~9~~8. The pharmaceutical composition of any preceding claim, wherein any one or more of the soluble CD52 glycoprotein, fusion protein, cell, cell population, cell culture medium and agent is capable of suppressing effector T-cell function and/or is capable of reducing an immune response.

~~10~~9. The pharmaceutical composition of claim ~~9~~8, wherein the immune response is an immune response to an autoantigen.

~~11~~10. The pharmaceutical composition of any preceding claim, wherein the fusion protein comprises a second protein which comprises an antibody fragment.

~~12~~11. The pharmaceutical composition of claim ~~11~~10, wherein the antibody fragment is an Fc.

~~13~~12. The pharmaceutical composition of any preceding claim, wherein the composition comprises one or more of the soluble CD52 glycoprotein, fusion protein, cell culture medium or agent, and is formulated for mucosal and/or transdermal administration.

~~14~~13. The pharmaceutical composition of any preceding claim which further comprises insulin and/or an autoantigen.

~~15~~14. A fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein wherein the second protein comprises an antibody fragment and/or a purification tag.

~~16~~15. The fusion protein of claim ~~15~~14, wherein the soluble CD52 glycoprotein comprises an amino acid sequence which ~~is at least 60%, 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.

~~17~~16. The fusion protein of claim ~~15~~14 or claim ~~16~~15, 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.

~~18~~17. The fusion protein of any one of claims ~~15~~14-~~17~~16, wherein the carbohydrate portion of soluble CD52 glycoprotein is linked to the asparagine (N) residue in SEQ ID NO: 3.

~~19~~18. The fusion protein of any one of claims ~~15~~14-~~18~~17, 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.

~~20~~19. The fusion protein of any one of claims ~~15~~14-~~19~~18, wherein the carbohydrate portion of soluble CD52 glycoprotein comprises one or more bi-, tri- or tetra-antennary sugars, which may be terminally sialylated.

~~21~~20. The fusion protein of any one of claims ~~15~~14-~~20~~19, which is capable of suppressing effector T-cell function and/or is capable of reducing an immune response.

~~22~~21. The fusion protein of claim ~~21~~20, wherein the immune response is an immune response to an autoantigen.

~~23. The fusion protein of any one of claims 15-22, wherein the second protein comprises an antibody fragment.~~

~~24~~22. The fusion protein of any one of claims ~~23~~14-21, wherein the antibody fragment is an Fc.

~~25~~23. An isolated or recombinant polynucleotide encoding the fusion protein of any one of claims ~~15~~14-~~24~~22.

~~26~~24. A vector comprising the polynucleotide of claim ~~25~~23.

~~27~~25. An isolated cell comprising the polynucleotide of claim ~~25~~23 or the vector of claim ~~26~~24.

~~28~~26. A method of producing the fusion protein of any one of claims ~~15~~14-~~24~~22, comprising expressing the polynucleotide of claim ~~25~~23 or vector of claim ~~26~~24 under glycosylation-permitting conditions.

~~29~~27. The method of claim ~~28~~26, wherein the glycosylation-permitting conditions comprise expressing the fusion protein in a host cell, such as a mammalian cell.

~~30~~28. Use of any one or more of:

i) soluble CD52 glycoprotein,

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein wherein the second protein comprises an antibody fragment and/or a purification tag;

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

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

x) the pharmaceutical composition of any one of claims 1-~~14~~13,

in the manufacture of a medicament for suppressing effector T-cell function and/or for reducing an immune response, such as an immune response to an autoantigen.

~~31. A method of treating or preventing a disease or condition mediated by effector T-cell function, inflammation or sepsis, in a subject, the method comprising administering a therapeutically effective amount of any one or more of:~~

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

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

~~x) the pharmaceutical composition of any one of claims 1-14,~~

~~to the subject.~~

~~32~~29. Any one or more of:

i) soluble CD52 glycoprotein,

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein wherein the second protein comprises an antibody fragment and/or a purification tag;

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

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

x) the pharmaceutical composition of any one of claims 1-~~14~~13,

for use in treating or preventing a disease or condition mediated by effector T-cell function, inflammation or sepsis.

~~33~~30. The use of any one or more of:

i) soluble CD52 glycoprotein,

ii) a fusion protein comprising soluble CD52 glycoprotein as a first protein, and a second protein wherein the second protein comprises an antibody fragment and/or a purification tag;

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

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

x) the pharmaceutical composition of any one of claims 1-~~14~~13,

in the manufacture of a medicament for the treatment or prevention of a disease or condition mediated by effector T-cell function, inflammation or sepsis.

~~34. The method of claim 31, the soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, cell population, cell culture medium, agent or pharmaceutical composition of claim 32, or the use of claim 33, wherein the disease mediated by effector T-cell function is an autoimmune disease, such as type I diabetes or rheumatoid arthritis.~~

~~35. The method of claim 31, the soluble CD52 glycoprotein, fusion protein, polynucleotide, vector, cell, cell population, cell culture medium, agent or pharmaceutical composition of claim 32, or the use of claim 33, wherein the condition mediated by effector T-cell function is an allograft rejection or a graft-versus-host reaction.~~

~~36. The method of claim 31, or the soluble CD52 glycoprotein, fusion protein, cell culture medium, agent or pharmaceutical composition of claim 32, wherein the soluble CD52 glycoprotein, fusion protein, cell culture medium, agent or composition is administered at a mucosal or transdermal site.~~

~~37~~31. The use of claim ~~33~~30, wherein the medicament is formulated for administration at a mucosal or transdermal site.

~~38~~32. A method of diagnosing a subject's susceptibility to developing a disease or condition mediated by effector T-cell function, inflammation or sepsis, 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 a disease or condition mediated by effector T-cell function, inflammation or sepsis.

~~39~~33. A method of diagnosing a subject's susceptibility to developing a disease or condition mediated by effector T-cell function, inflammation or 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 a disease or condition mediated by effector T-cell function, inflammation or sepsis.

~~40~~34. A method of diagnosing a subject's susceptibility to developing a disease or condition mediated by effector T-cell function, inflammation or 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 a disease or condition mediated by effector T-cell function, inflammation or sepsis.

~~41~~35. The method of claim ~~39~~33, 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.

~~42~~36. The method of any one of claims ~~38~~32-~~41~~35, wherein the sample ~~is~~was taken from a subject to which an antigen ~~has~~had been administered.

~~43~~37. The method of any one of claims ~~38~~32-~~42~~36, wherein the sample ~~is~~was taken from a local disease site in the subject.

~~44~~38. A method of determining a subject's suitability for entry into a drug screening trial, comprising performing the method of any one of claims 36-41 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.

~~45~~39. The method of claim ~~44~~38, wherein the drug screening trial is an anti-diabetic drug screening trial.

~~46~~40. 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.

~~47~~41. 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.