wherein X is any amino acid;

wherein (B^1) is any amino acid and wherein n is an integer from 0 to ~~3~~2; or

(ii) said oxidoreductase motif is selected from the group comprising: [CST]X$(Z_2)^+$C or CX$(Z_2)^+$[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid; or

(iii) said oxidoreductase motif is selected from the group comprising: [CST]$(Z_1)^+$XC; or C$(Z_1)^+$X[CST],

wherein $(Z_1)^+$ is a basic amino acid which is not H or R;

wherein X is any amino acid; or

(iv) said oxidoreductase motif is selected from the group comprising: [CST]XXC$(B^2)_m(Z_3)^+$, or CXX[CST]$(B^2)_m(Z_3)^+$,

Wherein $(Z_3)^+$ is K, R, or a non-natural basic amino acid such as L-ornithine,

wherein X is any amino acid;

wherein (B^2) is any amino acid and wherein m is an integer from 0 to ~~3~~2, with the proviso that when $(Z_3)^+$ is R, m is 0.

In a preferred example of said oxidoreductase motifs as described herein, when present, B^1 and/or B^2 are each independently selected from: H, K, or R, preferably H.

Particularly preferred examples of the disclosure comprise one of the following oxidoreductase motifs:

KCXXC, wherein X is any amino acid, preferably RCPYC, RCGHC, or RCHGC;

KCXXC, wherein X is any amino acid, preferably KCPYC, KCGHC, or KCHGC;

KHCXXC, wherein X is any amino acid, preferably RHCPYC, RHCGHC, or RHCHGC;

amino acid at its N-terminal end, i.e. immediately adjacent to the linker or oxidoreductase motif, more particularly in case the linker is absent or only comprises 1 or 2 amino acids.

In a further example of the disclosure, the T-cell epitope does not comprise a basic amino acid in position 1, 2 and/or 3 counted from its N-terminal end, i.e. immediately adjacent to the linker or oxidoreductase motif, more particularly in case the linker is absent or only comprises 1 or 2 amino acids.

In a further example of the disclosure, either one of X, (B^1), and/or (B^2) can be a basic amino acid. In another example, either one of X, (B^1), and/or (B^2) is any amino acid except for C, S, or T. In yet a further example, either one of X, (B^1), and/or (B^2) is any amino acid except for a basic amino acid.

The peptides of the present disclosure have the advantage that cytolytic CD4+ T cells which have been generated using these peptides have an increased IFN-gamma and sFasL production compared to prior art peptides. Also Granzyme B production in said CD4+ T cells is believed to be increased.

The increased expression levels of these markers are indications of a greater capacity of the peptides of the present disclosure to generate cytolytic CD4+ T cells compared to the prior art peptides.

In another aspect, the present disclosure refers to the immunogenic peptide as described herein, for use in medicine.

In another aspect, the present disclosure refers to the immunogenic peptide as described herein, for use in treating and/or prevention of an autoimmune disease, an infection with an intracellular pathogen, a tumor, an allograft rejection, or an immune response to a soluble allofactor, to an allergen exposure or to a viral vector used for gene therapy or gene vaccination.

In another aspect, the present disclosure refers to a use of the immunogenic peptide as described herein, in the manufacture of a medicament for treating and/or prevention of an autoimmune disease, an infection with an intracellular pathogen, a tumor, an allograft rejection, or an immune response to a soluble allofactor, to an allergen exposure or to a viral vector used for gene therapy or gene vaccination.

In another aspect, the present disclosure refers to a method for preparing an immunogenic peptide as described herein, comprising the steps of:

(a) providing a peptide sequence consisting of a T-cell epitope of said antigenic protein, and

(b) linking to said peptide sequence the oxidoreductase motif, such that said motif and said epitope are either adjacent to each other or separated by a linker of at most 7 amino acids.

In another aspect, the present disclosure refers to an *in vitro* method for obtaining a population of antigen-specific cytolytic CD4+ T cells, against APC presenting said antigen, the method comprising the steps of:

- providing peripheral blood cells;
- contacting said cells with an immunogenic peptide comprising:

a) an oxidoreductase motif,

b) a T-cell epitope of an antigenic protein, and

c) a linker between a) and b) of between 0 and 7 amino acids,

wherein:

(i) said oxidoreductase motif is selected from the group comprising:

$(Z_2)^+(B^1)_n$[CST]XXC or $(Z_2)^+(B^1)_n$CXX[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid;

wherein (B^1) is any amino acid and wherein n is an integer from 0 to 2; or

(ii) said oxidoreductase motif is selected from the group comprising: [CST]X$(Z_2)^+$C or CX$(Z_2)^+$[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid;

~~wherein (B^1) is any amino acid and wherein n is an integer from 0 to 3;~~ or

(iii) said oxidoreductase motif is selected from the group comprising: [CST]$(Z_1)^+$XC; or C$(Z_1)^+$X[CST],

wherein $(Z_1)^+$ is a basic amino acid which is not H or R;

wherein X is any amino acid; or

(iv) said oxidoreductase motif is selected from the group comprising: [CST]XXC$(B^2)_m(Z_3)^+$, or CXX[CST]$(B^2)_m(Z_3)^+$,

wherein $(Z_3)^+$ is K, R, or a non-natural basic amino acid such a L-ornithine,

wherein X is any amino acid;

wherein (B^2) is any amino acid and wherein m is an integer from 0 to ~~3~~2, with the proviso that when $(Z_3)^+$ is R, m is 0; and

- expanding said cells in the presence of IL-2.

In another aspect, the present disclosure refers to an *in vitro* method for obtaining a population of antigen-specific NKT cells, the method comprising the steps of:

- providing peripheral blood cells;
- contacting said cells with an immunogenic peptide comprising:

a) an oxidoreductase motif,

b) a T-cell epitope of an antigenic protein, and

c) a linker between a) and b) of between 0 and 7 amino acids,

wherein:

(i) said oxidoreductase motif is selected from the group comprising:

$(Z_2)^+(B^1)_n$[CST]XXC or $(Z_2)^+(B^1)_n$CXX[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid;

wherein (B^1) is any amino acid and wherein n is an integer from 0 to ~~3~~2; or

(ii) said oxidoreductase motif is selected from the group comprising: [CST]X$(Z_2)^+$C or CX$(Z_2)^+$[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid; or

(iii) said oxidoreductase motif is selected from the group comprising: [CST]$(Z_1)^+$XC; or C$(Z_1)^+$X[CST],

wherein $(Z_1)^+$ is a basic amino acid which is not H or R;

wherein X is any amino acid; or

(iv) said oxidoreductase motif is selected from the group comprising: [CST]XXC$(B^2)_m(Z_3)^+$, or CXX[CST]$(B^2)_m(Z_3)^+$,

wherein $(Z_3)^+$ is K, R, or a non-natural basic amino acid such a L-ornithine,

wherein X is any amino acid;

wherein (B^2) is any amino acid and wherein m is an integer from 0 to ~~3~~2, with the proviso that when $(Z_3)^+$ is R, m is 0; and

- expanding said cells in the presence of IL-2.

~~In another aspect, the present disclosure refers to a method for obtaining a population of antigen-specific cytolytic CD4+ T cells, against APC presenting said antigen, the method comprising the steps of:~~

~~providing an immunogenic peptide comprising:~~

~~a) an oxidoreductase motif,~~

~~b) a T-cell epitope of an antigenic protein, and~~

~~c) a linker between a) and b) of between 0 and 7 amino acids,~~

~~wherein:~~

~~(i) said oxidoreductase motif is selected from the group comprising:~~

~~$(Z_2)^+(B^1)_n$[CST]XXC or $(Z_2)^+(B^1)_n$CXX[CST];~~

~~wherein $(Z_2)^+$ is a basic amino acid which is not H;~~

~~wherein X is any amino acid;~~

~~wherein (B^1) is any amino acid and wherein n is an integer from 0 to 3; or~~

~~(ii) said oxidoreductase motif is selected from the group comprising: [CST]X$(Z_2)^+$C or CX$(Z_2)^+$[CST];~~

wherein $(Z_2)^+$ is a basic amino acid which is not H;
wherein X is any amino acid; or
(iii) said oxidoreductase motif is selected from the group comprising: [CST]$(Z_1)^+$XC; or C$(Z_1)^+$X[CST],
wherein $(Z_1)^+$ is a basic amino acid which is not H or R;
wherein X is any amino acid; or
(iv) said oxidoreductase motif is selected from the group comprising: [CST]XXC$(B^2)_m(Z_3)^+$, or CXX[CST]$(B^2)_m(Z_3)^+$,
wherein $(Z_3)^+$ is K, R, or a non-natural basic amino acid such a L-ornithine,
wherein X is any amino acid;
wherein (B^2) is any amino acid and wherein m is an integer from 0 to 3, with the proviso that when $(Z_3)^+$ is R, m is 0;
- administering said peptide to a subject; and
- obtaining said population of antigen-specific cytolytic CD4+ T cells from said subject.

In another aspect, the present disclosure refers to a method for obtaining a population of antigen-specific NKT cells, the method comprising the steps of:
- providing an immunogenic peptide comprising:
a) an oxidoreductase motif,
b) a T-cell epitope of an antigenic protein, and
c) a linker between a) and b) of between 0 and 7 amino acids,
wherein:
(i) said oxidoreductase motif is selected from the group comprising:
$(Z_2)^+(B^1)_n$[CST]XXC or $(Z_2)^+(B^1)_n$CXX[CST];
wherein $(Z_2)^+$ is a basic amino acid which is not H;
wherein X is any amino acid;
wherein (B^1) is any amino acid and wherein n is an integer from 0 to 3; or
(ii) said oxidoreductase motif is selected from the group comprising: [CST]X$(Z_2)^+$C or CX$(Z_2)^+$[CST];
wherein $(Z_2)^+$ is a basic amino acid which is not H;
wherein X is any amino acid; or
(iii) said oxidoreductase motif is selected from the group comprising: [CST]$(Z_1)^+$XC; or C$(Z_1)^+$X[CST],
wherein $(Z_1)^+$ is a basic amino acid which is not H or R;
wherein X is any amino acid; or
(iv) said oxidoreductase motif is selected from the group comprising: [CST]XXC$(B^2)_m(Z_3)^+$, or CXX[CST]$(B^2)_m(Z_3)^+$,
wherein $(Z_3)^+$ is K, R, or a non-natural basic amino acid such a L-ornithine,
wherein X is any amino acid;

~~wherein (B^2) is any amino acid and wherein m is an integer from 0 to 3, with the proviso that when (Z_3)$^+$ is R, m is 0;~~

~~administering said peptide to a subject; and~~

~~obtaining said population of antigen-specific NKT cells from said subject.~~

In another aspect, the present disclosure refers to the population of antigen-specific cytolytic CD4+ T cells or NKT cells obtainable by the method as described herein for use in the treatment and/or prevention of an autoimmune disease, an infection with an intracellular pathogen, a tumor, an allograft rejection, or an immune response to a soluble allofactors, to an allergen exposure or to a viral vector used for gene therapy or gene vaccination.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1: represents the kinetics of the redox activities of immunogenic peptides comprising a CHGC motif and an insulin T cell epitope. The basic amino acid is inserted at the N-terminus of the oxidoreductase motif, and the initial velocities of the redox activities are followed for 10 minutes. Peptides with oxidoreductase motifs without any charged amino acid or with an H at their N-terminus are used as control peptides. See table 1 for details.

Figure 2: represents the kinetics of the redox activities of immunogenic peptides comprising a CPYC motif and a tetanus toxin T cell epitope. The basic amino acid is inserted at the N-terminus of the oxidoreductase motif, and the initial velocities of the redox activities are followed for 10 minutes. Peptides with oxidoreductase motifs without any charged amino acid or with an H at their N-terminus are used as control peptides. See table 2 for details.

Figure 3: represents the kinetics of the redox activities of immunogenic peptides comprising a CPYC motif and a MOG T cell epitope. The basic amino acid is inserted at the N-terminus of the

CLAIMS

1. An immunogenic peptide, said immunogenic peptide comprising:

a) an oxidoreductase motif,

b) a T-cell epitope of an antigenic protein, and

c) a linker between a) and b) of between 0 and 7 amino acids

wherein:

(i) said oxidoreductase motif is selected from the group comprising:

$(Z_2)^+(B^1)_n$[CST]XXC or $(Z_2)^+(B^1)_n$CXX[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid;

wherein (B^1) is any amino acid and wherein n is an integer from 0 to ~~3~~2; or

(ii) said oxidoreductase motif is selected from the group comprising: [CST]X$(Z_2)^+$C or CX$(Z_2)^+$[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid; or

(iii) said oxidoreductase motif is selected from the group comprising: [CST]$(Z_1)^+$XC; or C$(Z_1)^+$X[CST],

wherein $(Z_1)^+$ is a basic amino acid which is not H or R;

wherein X is any amino acid; or

(iv) said oxidoreductase motif is selected from the group comprising: [CST]XXC$(B^2)_m(Z_3)^+$, or CXX[CST]$(B^2)_m(Z_3)^+$,

wherein $(Z_3)^+$ is K, R, or a non-natural basic amino acid such as L-ornithine,

wherein X is any amino acid;

wherein (B^2) is any amino acid and wherein m is an integer from 0 to ~~3~~2, with the proviso that when $(Z_3)^+$ is R, m is 0.

2. The immunogenic peptide according to claim 1, wherein $(Z_1)^+$ is selected from the group comprising: K or a non-natural basic amino acid and/or wherein either one of $(Z_2)^+$ and/or $(Z_3)^+$ each individually is selected from the group comprising: K, R or a non-natural basic amino acid.

3. The immunogenic peptide according to claim 1 or 2, wherein either one of $(Z_1)^+$, $(Z_2)^+$, and/or $(Z_3)^+$ is K or L-ornithine.

4. The immunogenic peptide according to any one of claims 1 to 3, wherein said T cell epitope of an antigenic protein is an NKT cell epitope or an MHC class II T cell epitope.

5. The immunogenic peptide according to any one of claims 1 to 4, wherein said epitope has a length of between 7 and 30 amino acids, preferably between 7 and 25 amino acids, more preferably between 7 and 20 amino acids.

6. The immunogenic peptide according to any one of claims 1 to 5, having a length of between 11 and 50 amino acids, preferably between 11 and 40 amino acids, more preferably between 11 and 30 amino acids.

7. The immunogenic peptide according to any one of claims 1 to 6, wherein said antigenic protein is an auto-antigen, a soluble allofactor, an alloantigen shed by the graft, an antigen of an intracellular pathogen, an antigen of a viral vector used for gene therapy or gene vaccination, a tumor-associated antigen or an allergen.

8. The immunogenic peptide according to any one of claims 1 to 7, wherein at least one X in the motif is P or Y.

9. The immunogenic peptide according to any one of claims 1 to 8, wherein the linker is of between 0 and 4 amino acids.

10. The immunogenic peptide according to any one of claims 1 to 9, wherein said oxidoreductase motif does not naturally occur within a region of 11 amino acids N-terminally or C-terminally of the T-cell epitope in said antigenic protein.

11. The immunogenic peptide according to any one of claims 1 to 10, wherein the T-cell epitope does not naturally comprise said oxidoreductase motif.

12. The immunogenic peptide according to any one of claims 1 to 11, for use in medicine.

13. The immunogenic peptide according to any one of claims 1 to 11, for use in treating and/or prevention of an autoimmune disease, an infection with an intracellular pathogen, a tumor, an allograft rejection, or an immune response to a soluble allofactor, to an allergen exposure or to a viral vector used for gene therapy or gene vaccination.

14. A use of the immunogenic peptide according to any one of claims 1 to 11, in the manufacture of a medicament for treating and/or prevention of an autoimmune disease, an infection with an intracellular pathogen, a tumor, an allograft rejection, or an immune response to

a soluble allofactor, to an allergen exposure or to a viral vector used for gene therapy or gene vaccination.

15. A method for preparing an immunogenic peptide according to any one of claims 1 to 11, comprising the steps of:

(a) providing a peptide sequence consisting of a T-cell epitope of said antigenic protein, and

(b) linking to said peptide sequence the oxidoreductase motif, such that said motif and said epitope are either adjacent to each other or separated by a linker of at most 7 amino acids.

16. An *in vitro* method for obtaining a population of antigen-specific cytolytic CD4+ T cells, against APC presenting said antigen, the method comprising the steps of:

- providing peripheral blood cells;
- contacting said cells with an immunogenic peptide comprising:

a) an oxidoreductase motif,

b) a T-cell epitope of an antigenic protein, and

c) a linker between a) and b) of between 0 and 7 amino acids,

wherein:

(i) said oxidoreductase motif is selected from the group comprising:

$(Z_2)^+(B^1)_n$[CST]XXC or $(Z_2)^+(B^1)_n$CXX[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid;

wherein (B^1) is any amino acid and wherein n is an integer from 0 to 2; or

(ii) said oxidoreductase motif is selected from the group comprising: [CST]X$(Z_2)^+$C or C$X(Z_2)^+$[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid;

~~wherein (B^1) is any amino acid and wherein n is an integer from 0 to 3;~~ or

(iii) said oxidoreductase motif is selected from the group comprising: [CST]$(Z_1)^+$XC; or C$(Z_1)^+$X[CST],

wherein $(Z_1)^+$ is a basic amino acid which is not H or R;

wherein X is any amino acid; or

(iv) said oxidoreductase motif is selected from the group comprising: [CST]XXC$(B^2)_m(Z_3)^+$, or CXX[CST]$(B^2)_m(Z_3)^+$,

wherein $(Z_3)^+$ is K, R, or a non-natural basic amino acid such a L-ornithine,

wherein X is any amino acid;

wherein (B^2) is any amino acid and wherein m is an integer from 0 to ~~3~~2, with the proviso that when $(Z_3)^+$ is R, m is 0; and

- expanding said cells in the presence of IL-2.

17. An *in vitro* method for obtaining a population of antigen-specific NKT cells, the method comprising the steps of:

- providing peripheral blood cells;
- contacting said cells with an immunogenic peptide comprising:

a) an oxidoreductase motif,

b) a T-cell epitope of an antigenic protein, and

c) a linker between a) and b) of between 0 and 7 amino acids,

wherein:

(i) said oxidoreductase motif is selected from the group comprising:

$(Z_2)^+(B^1)_n$[CST]XXC or $(Z_2)^+(B^1)_n$CXX[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid;

wherein (B^1) is any amino acid and wherein n is an integer from 0 to ~~3~~2; or

(ii) said oxidoreductase motif is selected from the group comprising: [CST]X$(Z_2)^+$C or C$X(Z_2)^+$[CST];

wherein $(Z_2)^+$ is a basic amino acid which is not H;

wherein X is any amino acid; or

(iii) said oxidoreductase motif is selected from the group comprising: [CST]$(Z_1)^+$XC; or C$(Z_1)^+$X[CST],

wherein $(Z_1)^+$ is a basic amino acid which is not H or R;

wherein X is any amino acid; or

(iv) said oxidoreductase motif is selected from the group comprising: [CST]XXC$(B^2)_m(Z_3)^+$, or CXX[CST]$(B^2)_m(Z_3)^+$,

wherein $(Z_3)^+$ is K, R, or a non-natural basic amino acid such a L-ornithine,

wherein X is any amino acid;

wherein (B^2) is any amino acid and wherein m is an integer from 0 to ~~3~~2, with the proviso that when $(Z_3)^+$ is R, m is 0; and

- expanding said cells in the presence of IL-2.

~~18. A method for obtaining a population of antigen-specific cytolytic CD4+ T cells, against APC presenting said antigen, the method comprising the steps of:~~

~~providing an immunogenic peptide comprising:~~

~~a) an oxidoreductase motif,~~

~~b) a T-cell epitope of an antigenic protein, and~~

~~c) a linker between a) and b) of between 0 and 7 amino acids,~~

~~wherein:~~

(i) said oxidoreductase motif is selected from the group comprising: $(Z_2)^+(B^1)_n$[CST]XXC or $(Z_2)^+(B^1)_n$CXX[CST];
wherein $(Z_2)^+$ is a basic amino acid which is not H;
wherein X is any amino acid;
wherein (B^1) is any amino acid and wherein n is an integer from 0 to 3; or
(ii) said oxidoreductase motif is selected from the group comprising: [CST]X$(Z_2)^+$C or C$X(Z_2)^+$[CST];
wherein $(Z_2)^+$ is a basic amino acid which is not H;
wherein X is any amino acid; or
(iii) said oxidoreductase motif is selected from the group comprising: [CST]$(Z_1)^+$XC; or C$(Z_1)^+$X[CST],
wherein $(Z_1)^+$ is a basic amino acid which is not H or R;
wherein X is any amino acid; or
(iv) said oxidoreductase motif is selected from the group comprising: [CST]XXC$(B^2)_m(Z_3)^+$, or CXX[CST]$(B^2)_m(Z_3)^+$,
wherein $(Z_3)^+$ is K, R, or a non-natural basic amino acid such a L-ornithine,
wherein X is any amino acid;
wherein (B^2) is any amino acid and wherein m is an integer from 0 to 3, with the proviso that when $(Z_3)^+$ is R, m is 0;
administering said peptide to a subject; and
obtaining said population of antigen-specific cytolytic CD4+ T cells from said subject.

19. A method for obtaining a population of antigen-specific NKT cells, the method comprising the steps of:
providing an immunogenic peptide comprising:
a) an oxidoreductase motif,
b) a T-cell epitope of an antigenic protein, and
c) a linker between a) and b) of between 0 and 7 amino acids,
wherein:
(i) said oxidoreductase motif is selected from the group comprising: $(Z_2)^+(B^1)_n$[CST]XXC or $(Z_2)^+(B^1)_n$CXX[CST];
wherein $(Z_2)^+$ is a basic amino acid which is not H;
wherein X is any amino acid;
wherein (B^1) is any amino acid and wherein n is an integer from 0 to 3; or
(ii) said oxidoreductase motif is selected from the group comprising: [CST]X$(Z_2)^+$C or C$X(Z_2)^+$[CST];
wherein $(Z_2)^+$ is a basic amino acid which is not H;
wherein X is any amino acid; or

~~(iii) said oxidoreductase motif is selected from the group comprising: [CST]$(Z_1)^+$XC; or C$(Z_1)^+$X[CST],~~

~~wherein $(Z_1)^+$ is a basic amino acid which is not H or R;~~

~~wherein X is any amino acid; or~~

~~(iv) said oxidoreductase motif is selected from the group comprising: [CST]XXC$(B^2)_m(Z_3)^+$, or CXX[CST]$(B^2)_m(Z_3)^+$,~~

~~wherein $(Z_3)^+$ is K, R, or a non-natural basic amino acid such a L-ornithine,~~

~~wherein X is any amino acid;~~

~~wherein (B^2) is any amino acid and wherein m is an integer from 0 to 3, with the proviso that when $(Z_3)^+$ is R, m is 0;~~

~~administering said peptide to a subject; and~~

~~obtaining said population of antigen-specific NKT cells from said subject.~~

~~20~~18. The population of antigen-specific cytolytic CD4+ T cells or NKT cells obtainable by the method of ~~any one of~~ claim~~s~~ 16 ~~to 19~~ or 17 for use in the treatment and/or prevention of an autoimmune disease, an infection with an intracellular pathogen, a tumor, an allograft rejection, or an immune response to a soluble allofactors, to an allergen exposure or to a viral vector used for gene therapy or gene vaccination.