

The disclosure relates to peptides with a length of between 12 and 50 amino acids, comprising the tetrapeptide sequence Cxx[CST] [SEQ ID NO: 1] or [CST]xxC [SEQ ID NO: 2] (i.e. the redox motif) and, separated from this tetrapeptide by 0 to 5 amino acids, preferably by 0 to 4 amino acids (i.e. by a linker), the sequence
 5 LALEGLSLQK [SEQ ID NO: 3] (i.e. the epitope).

Examples of these peptides comprise the sequence Cxx[CST]SLQPLALEGLSLQK [SEQ ID NO: 4] or [CST]xxCSLQPLALEGLSLQK [SEQ ID NO:5].

One aspect of the disclosure relates to an isolated immunogenic peptide with a length of between 12 and 50 amino acids, comprising the sequence
 10 Cxx[CST]SLQPLALEGLSLQK [SEQ ID NO: 4] or [CST]xxCSLQPLALEGLSLQK [SEQ ID NO:5], wherein x is any amino acid, and wherein [CST] is any one of C, S or T.

Other examples of these peptides comprise the sequence CxxCSLQPLALEGLSLQK [SEQ ID NO: 6].

Other examples of these peptides comprise the sequence
 15 HCxx[CST]SLQPLALEGLSLQK [SEQ ID NO:7] or H[CST]xxCSLQPLALEGLSLQK [SEQ ID NO:8].

Other examples of these peptides comprise the sequence HCxxCSLQPLALEGLSLQK [SEQ ID NO: 9].

Other examples of these peptides comprise the Cxx[CST] [SEQ ID NO: 1] or
 20 [CST]xxC [SEQ ID NO: 2] redox motif sequence and the sequence SLQPLALEGLSLQKRG [SEQ ID NO: 20].

Specific examples of these peptides consist of the sequence

Cxx[CST]SLQPLALEGLSLQK [SEQ ID NO: 4],
 [CST]xxCSLQPLALEGLSLQK [SEQ ID NO: 5],
 25 CxxCSLQPLALEGLSLQK [SEQ ID NO:6],
 HCxx[CST]SLQPLALEGLSLQK [SEQ ID NO:7],
 H[CST]xxCSLQPLALEGLSLQK [SEQ ID NO:8], or
 HCxxCSLQPLALEGLSLQK [SEQ ID NO:9].

Other specific examples of these peptides consist of the sequence

30 Cxx[CST]SLQPLALEGLSLQKRG [SEQ ID NO: 10],
 [CST]xxCSLQPLALEGLSLQKRG [SEQ ID NO: 11],
 CxxCSLQPLALEGLSLQKRG [SEQ ID NO: 12],
 HCxx[CST]SLQPLALEGLSLQKRG [SEQ ID NO:13],
 H[CST]xxCSLQPLALEGLSLQKRG [SEQ ID NO:14], or
 35 HCxxCSLQPLALEGLSLQKRG [SEQ ID NO: 15].

In specific examples of these sequences Cxx[CST] [SEQ ID NO: 1] is CPY[CST] [SEQ ID NO: 16], [CST]xxC [SEQ ID NO: 2] is [CST]PYC [SEQ ID NO: 17], more specific CxxC [SEQ ID NO: 18] is CPYC [SEQ ID NO:19].

A specific example is the peptide HCPYCSLQPLALEGSLQKRG [SEQ ID NO: 26]

In the above examples the redox motif is at the N terminal side of the epitope.

In an alternative set of examples the peptides have the redox motif at the C
5 terminal side of the epitope.

Another aspect of the disclosure relates to any one of the peptides as disclosed above for use as a medicament. Another aspect of the disclosure relates to any one of the peptides as disclosed above for use in the treatment of type 1 diabetes.

10 Another aspect of the disclosure relates to use of the peptide as disclosed above in the manufacture of a medicament for the treatment of type 1 diabetes. The peptides can also be for reducing the symptoms of type 1 diabetes.

Another aspect relates to pharmaceutical compositions comprising any one of the peptides as disclosed above and a pharmaceutically acceptable carrier.

15 Another aspect relates to an in vitro method for the generation of a population of cytolytic CD4+ T cells, against APC presenting insulin epitopes, comprising the steps of:

- providing peripheral blood cells;
- contacting said cells in vitro with any one of the immunogenic peptides as
20 disclosed above; and
- expanding said cells in the presence of IL-2.

Another aspect relates to a population of cells cytolytic CD4+ T cells, against APC presenting insulin epitopes, obtainable by the above method. Another aspect
25 relates to a population of cells cytolytic CD4+ T cells, against APC insulin presenting epitopes obtainable by the above method for use as a medicament.

There is also provided a population of cells obtainable by the above method for use in the treatment or prevention of type 1 diabetes. Another aspect relates to a population of cytolytic CD4+ T cells, against APC presenting insulin epitopes,
30 obtainable by the above method, for use in the treatment of type 1 diabetes. Another aspect relates to use of a population of cytolytic CD4+ T cells, against APC presenting insulin epitopes as disclosed above in the manufacture of a medicament for the treatment of type 1 diabetes.

Another aspect relates to the isolated immunogenic peptide as disclosed above, for
35 use in treatment of type 1 diabetes, or for reducing the symptoms of type 1 diabetes. Another aspect relates to use of the isolated immunogenic peptide as disclosed above in the manufacture of a medicament for the treatment of type 1 diabetes, or for reducing the symptoms of type 1 diabetes.

CLAIMS

1. An isolated immunogenic peptide with a length of between 12 and 50 amino acids, comprising the sequence Cxx[CST]SLQPLALEGSLQK [SEQ ID NO: 4] or [CST]xxCSLQPLALEGSLQK [SEQ ID NO:5], wherein x is any amino acid, and wherein [CST] is any one of C, S or T.
2. The peptide according to claim 1, comprising the sequence CxxCSLQPLALEGSLQK [SEQ ID NO: 6].
3. The peptide according to claim 1, comprising the sequence HCxx[CST]SLQPLALEGSLQK [SEQ ID NO:7] or H[CST]xxCSLQPLALEGSLQK [SEQ ID NO:8].
4. The peptide according to any one of claims 1 to 3, comprising the sequence HCxxCSLQPLALEGSLQK [SEQ ID NO: 9].
5. The peptide according to any one of claims 1 to 4, consisting of amino acid sequence HCPYCSLQPLALEGSLQKRG [SEQ ID NO: 26].
6. The peptide according to any one of claims 1 to 5 for use as a medicament.
7. The peptide according to any one of claims 1 to 5 for use in the treatment of type 1 diabetes.
8. Use of the peptide according to any one of claims 1 to 5 in the manufacture of a medicament for the treatment of type 1 diabetes.
9. A pharmaceutical composition comprising the peptide of any one of claims 1 to 5 and a pharmaceutically acceptable carrier.
10. An in vitro method for the generation of a population of cytolytic CD4+ T cells, against APC presenting insulin epitopes, comprising the steps of:
 - providing peripheral blood cells;
 - contacting said cells in vitro with the peptide of any one of claims 1 to 5; and
 - expanding said cells in the presence of IL-2.

11. A population of cytolytic CD4+ T cells, against APC presenting insulin epitopes, obtainable by the method of claim 10.
12. A population of cytolytic CD4+ T cells, against APC presenting insulin epitopes, obtainable by the method of claim 10, for use as a medicament.
13. A population of cytolytic CD4+ T cells, against APC presenting insulin epitopes, obtainable by the method of claim 10, for use in the treatment of type 1 diabetes.
14. Use of a population of cytolytic CD4+ T cells, against APC presenting insulin epitopes according to claim 11 in the manufacture of a medicament for the treatment of type 1 diabetes.
15. The isolated immunogenic peptide according to claim 5, for use in treatment of type 1 diabetes, or for reducing the symptoms of type 1 diabetes.
16. Use of the isolated immunogenic peptide according to claim 5 in the manufacture of a medicament for the treatment of type 1 diabetes, or for reducing the symptoms of type 1 diabetes.