response in the host sufficient to eliminate the cells that are transduced by the lentiviral vectors. The elimination of transduced cells eliminates the persistence of the lentiviral vector in the host, and possible secondary effects of the vector. In order for the transduced cells to be eliminated, expression is required in non-dendritic cells at a level that allows elimination by the immune response.

At the same time, the promoter should maximize immune stimulation through the key cells (i.e., dendritic cells) involved in the activation of naïve and memory T cells, and should minimize the risk of insertional mutagenesis and genotoxicity in stem cells, leading to malignancies. Thus, the promoter should have sufficiently high activity in dendritic and other cells, but not contain an enhancer. Based on these criteria, viral promoters, such as the CMV promoter, are not ideal because of the presence of strong enhancers. These criteria are summarized as follows:

1. high expression in antigen presenting cells, including dendritic cells, to induce maximal immune responses;
2. expression in other transduced cell types sufficient for elimination by the induced immune response; and
3. lack of an enhancer element to avoid insertional effects.

Thus, a need exists in the art for improved vectors. The present invention fulfils these needs in the art.

SUMMARY ~~OF THE INVENTION~~

The ~~invention~~ disclosure encompasses compositions comprising lentiviral vectors and methods of using the vectors. In one aspect, the present invention refers to a lentiviral vector comprising a transgene sequence encoding an immunogenic polypeptide, wherein the transgene sequence is under the transcriptional control of a MHC class I promoter In one ~~embodiment~~example, the ~~invention~~ disclosure encompasses a lentiviral vector comprising a transgene sequence encoding an immunogenic polypeptide, wherein the transgene sequence is under the transcriptional control of a MHC class I promoter; wherein the vector induces a greater CTL response in vivo against the encoded immunogenic polypeptide than a vector in which the transgene sequence is under the transcriptional control of a CMV promoter.

Preferably, the MHC class I promoter is an HLA-A2 promoter, an HLA-B7 promoter, an HLA-Cw5 promoter, an HLA-E promoter, or an HLA-F promoter.

In various ~~embodiments~~examples, the promoter sequence comprises a polynucleotide sequence that shares more than 90%, preferably more than 95%,

more preferably more than 99% identity with the promoter sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, or SEQ ID NO:5.

In various ~~embodiments~~examples, the vector comprises an LTR that is deleted for the promoter and enhancer of U3, a cPPT/CTS sequence from a lentivirus, a Ψ (psi) sequence, and/or two lentiviral LTRs.

In a preferred ~~embodiment~~example, the lentiviral vector does not contain an enhancer.

The immunogenic polypeptide encoded by the transgene comprises antigen(s) from Gag, Pol and/or Nef proteins from HIV virus. The antigen can be at least one tumour antigen.

The ~~invention~~ disclosure further encompasses an isolated host cell comprising the lentiviral vector of the invention. In one aspect, the present invention refers to an isolated host cell comprising the lentiviral vector as described herein.

The ~~invention~~ disclosure further encompasses methods for producing a lentiviral vector particle. In one aspect, the present invention refers to an *in vitro* method for producing a lentiviral vector particle comprising the steps of transfecting a suitable host cell with the lentiviral vector as described herein; transfecting said host cell with a packaging plasmid vector containing viral DNA sequences encoding at least structural and polymerase activities of a retrovirus; culturing said transfected host cell in order to obtain expression and packaging of said lentiviral vector into lentiviral vector particles; and harvesting the lentiviral vector particles resulting from the expression and packaging of the previous step in said cultured host cells. In another aspect, the present invention refers to a lentiviral vector particle comprising the lentiviral vector as described herein. In yet another example, the present invention refers to a lentiviral vector particle comprising at least the following sequence elements: cPPT/CTS polynucleotide sequence; an LTR that is deleted for the promoter and enhancer of U3; and a transgene sequence under control of an MHC class I promoter. Such methods can comprise the steps of transfecting a suitable host cell with the lentiviral vector; transfecting the host cell with a packaging plasmid vector containing viral DNA sequences encoding at least structural and integrase proteins of a retrovirus; culturing said transfected host cell in order to obtain expression and packaging of

said lentiviral vector into lentiviral vector particles; and harvesting the lentiviral vector particles resulting from the expression and packaging in said cultured host cells.

The ~~invention~~ disclosure further encompasses lentiviral vector particles comprising the lentiviral vector of the ~~invention~~disclosure. The lentiviral vector particle can comprise a cPPT/CTS polynucleotide sequence; a LTR that is deleted for the promoter and enhancer of U3; and/or a transgene sequence under control of an MHC class I promoter. Preferably, the promoter sequence comprises a polynucleotide sequence that shares more than 90%, preferably more than 95%, more preferably more than 99% identity with the promoter sequence of SEQ ID NO.1, , SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, or SEQ ID NO:5.

The ~~invention~~ discosure further encompasses compositions comprising a lentiviral vector or lentiviral vector particle according to the invention for use as a medicament or vaccine. In one aspect, the present invention refers to a lentiviral vector or lentiviral vector particle as described herein for use as a medicament or vaccine.

The ~~invention~~ disclosure further encompasses methods for inducing a T-cell response comprising administering to a patient a lentiviral vector particle

CLAIMS

We claim:

1. A lentiviral vector comprising a transgene sequence encoding an immunogenic polypeptide, wherein the transgene sequence is under the transcriptional control of a MHC class I promoter.

2. The lentiviral vector of claim 1, wherein the vector induces a greater CTL response *in vivo* against the encoded immunogenic polypeptide than a vector in which the transgene sequence is under the transcriptional control of a CMV promoter.

3. The lentiviral vector of claim 1 or 2, wherein the MHC class I promoter is an HLA-A2 promoter, an HLA-B7 promoter, an HLA-Cw5 promoter, an HLA-F, or an HLA-E promoter.

4. The lentiviral vector of claim 1 or 2, wherein said promoter sequence comprises a polynucleotide sequence that shares more than 90%, preferably more than 95%, more preferably more than 99% identity with the promoter sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, or SEQ ID NO:5

5. The lentiviral vector of claim any one of claims 1-4, comprising an LTR that is deleted for the promoter and enhancer of U3, a cPPT/CTS sequence from a lentivirus, a Ψ (psi) sequence, or two lentiviral LTRs.

6. The lentiviral vector of any one of claims 1-5, wherein the lentiviral vector does not contain an enhancer.

7. The lentiviral vector of any one of claims 1-6, wherein said immunogenic polypeptide comprises antigen(s) from Gag, Pol and/or Nef proteins from HIV virus or at least one tumour antigen.

8. An isolated host cell comprising the lentiviral vector of any one of claims 1-7.

9. An *in vitro* method for producing a lentiviral vector particle comprising the steps of:

a) transfecting a suitable host cell with the lentiviral vector of any one of claims 1-7;

b) transfecting said host cell with a packaging plasmid vector containing viral DNA sequences encoding at least structural and polymerase activities of a retrovirus;

c) culturing said transfected host cell in order to obtain expression and packaging of said lentiviral vector into lentiviral vector particles; and

d) harvesting the lentiviral vector particles resulting from the expression and packaging of step c) in said cultured host cells.

10. A lentiviral vector particle comprising the lentiviral vector of any one of claims 1-7.

11. A lentiviral vector particle comprising at least the following sequence elements:

a) cPPT/CTS polynucleotide sequence;

b) an LTR that is deleted for the promoter and enhancer of U3; and

c) a transgene sequence under control of an MHC class I promoter.

12. The lentiviral vector particle of claim 11, wherein said promoter sequence comprises a polynucleotide sequence that shares more than 90%, preferably more than 95%, more preferably more than 99% identity with the promoter sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, or SEQ ID NO:5.

13. A lentiviral vector or lentiviral vector particle according to any one of claims 1-7 and 11-12 for use as a medicament or vaccine.