Moreover, contrary to exogenous infectious retroviruses, HERVs are present in the DNA of all cells from each human individual and, therefore, therapeutic molecules classically used for treating human retroviruses cannot eliminate the corresponding provirus within a sub-population of reservoir cells. Many cellular and genetic constraints on these endogenous elements also make them controlled by non-retroviral molecular mechanisms, thus escaping from classical retroviral pathways. Among these various mechanisms, an involvement of gene silencing, of gene control by cellular promoter/enhancer or of genetic recombination between HERV sequences and cellular genes are known. Such features are not expected with classical exogenous retroviruses and therefore are not accessible to presently existing anti-retroviral therapy.

In such conditions, treatments of classical exogenous retroviruses cannot expect to fully control pathogenic HERV expression and, consequently, to have optimal therapeutic efficiency, if any, on HERV-associated diseases.

There is thus a long time felt unfulfilled need for a novel antiretroviral therapeutic strategy targeting the HERV viruses.

SUMMARY

The present disclosure relates to a use of an antibody, a fragment or a derivative thereof, in the manufacture of an antiretroviral drug targeting a virus belonging to human endogenous retroviruses (HERV), wherein said antibody, fragment or derivative is directed against HERV-W Envelope protein (HERV-W Env).

The present disclosure also relates to a use of a composition comprising:

- an antibody, a fragment, or a derivative thereof as defined herein; and
- a retroviral reverse-transcriptase inhibitory drug;

in the manufacture of an antiretroviral drug targeting a virus belonging to human endogenous retroviruses type W (HERV-W).

The present disclosure relates to a use of a composition comprising:

- an antibody, a fragment or a derivative thereof as defined herein; and
- a retroviral reverse-transcriptase inhibitory drug;

in the manufacture of a medicament for preventing and/or treating a disease selected from the group consisting of multiple sclerosis (MS), schizophrenia (SZ), bipolar disorder (BP), unipolar or psychotic depression, clinically isolated syndrome (CIS, with neurological symptom), chronic inflammatory demyelinating polyneuropathy (CIDP), epilepsy, psoriasis, cancer, inflammatory pancreatitis and diabetes such as type 1 or type 2 diabetes.

The present disclosure also relates to a use of a an antibody, a fragment or a derivative thereof directed against HERV-W Envelope protein (HERV-W Env) as defined herein and a retroviral reverse-transcriptase inhibitory drug in the manufacture of a combined preparation for treating a disease selected from the group consisting of multiple sclerosis (MS), schizophrenia (SZ), bipolar disorder (BP), unipolar or psychotic depression, clinically isolated syndrome (CIS, with neurological symptom), chronic inflammatory demyelinating polyneuropathy (CIDP), epilepsy, psoriasis, cancer, inflammatory pancreatitis and diabetes such as type 1 or type 2 diabetes, wherein said combined preparation is formulated for simultaneous, separate or sequential use.

The present disclosure also relates to a kit comprising at least two oligonucleotides selected from the group consisting of SEQ ID No: 11 to 28.

The present disclosure further relates to a use of an antibody, a fragment or a derivative thereof directed against HERV-W Envelope protein (HERV-W Env) in the manufacture of an antiretroviral drug for targeting a virus belonging to human endogenous retroviruses (HERV) in a patient suffering from an HERV-W associated disease, wherein said patient is identified by a method comprising a step i) of detecting and/or quantifying HERV-W in a biological sample of said patient.

In one aspect, there is provided the use of a composition comprising: an antibody; and a retroviral reverse-transcriptase inhibitory drug; in the manufacture of an antiretroviral drug targeting a virus belonging to human endogenous retroviruses type W (HERV-W); wherein said antibody is directed against HERV-W Envelope protein (HERV-W Env).

Another aspect relates to the use of a an antibody directed against HERV-W Envelope protein (HERV-W Env) as defined above and a retroviral reverse-transcriptase inhibitory drug in the manufacture of a combined preparation for treating a disease selected from the group consisting of multiple sclerosis (MS), schizophrenia (SZ), bipolar disorder (BP), unipolar or psychotic depression, clinically isolated syndrome (CIS, with neurological symptom), chronic

inflammatory demyelinating polyneuropathy (CIDP), epilepsy, psoriasis, cancer, inflammatory pancreatitis and diabetes such as type 1 or type 2 diabetes, wherein said combined preparation is formulated for simultaneous, separate or sequential use.

Another aspect relates to the use of an antibody directed against HERV-W Envelope protein (HERV-W Env) as defined above and a retroviral reverse-transcriptase inhibitory drug in the manufacture of a combined preparation for treating a disease selected from the group consisting of Multiple Sclerosis (MS) and Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), wherein said combined preparation is formulated for simultaneous, separate or sequential use.

Another aspect relates to a composition comprising: an antibody as defined herein; and a retroviral reverse-transcriptase inhibitory drug.

The inventors have surprisingly found out that an unexpected anti-HERV effect targeting endogenous elements from the HERV-W family can reduce and inhibit HERV-W expression. Therefore, **in a first aspect**, the invention relates to an antibody, a fragment or a derivative thereof for use as an antiretroviral drug targeting a virus belonging to a human endogenous retrovirus (HERV), wherein said antibody is directed against HERV-W Envelope protein (HERV-W Env). Preferably, said antibody, fragment or derivative is for preventing and/or treating an HERV-W associated disease. More preferably, said antibody is for preventing and/or treating Multiple Sclerosis (MS) or Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). More preferably, said antibody is a monoclonal humanized antibody, wherein the heavy chain (HC) has the amino acid sequence as set forth in SEQ ID No: 9 and the light chain (LC) has the amino acid sequence set forth in SEQ ID No: 10.

CLAIMS

1. Use of a composition comprising:

- an antibody; and
- a retroviral reverse-transcriptase inhibitory drug;

in the manufacture of an antiretroviral drug targeting a virus belonging to human endogenous retroviruses type W (HERV-W);

wherein said antibody is directed against HERV-W Envelope protein (HERV-W Env).

2. The use according to claim **1**, wherein said antibody is able to:

- suppress or inhibit totally or partially the replication of a virus belonging to the human endogenous retroviruses type W (HERV-W) family; or
- suppress or inhibit totally or partially the expression of a virus belonging to human endogenous retroviruses type W family, or the expression of the envelope protein of said virus.

3. The use according to claim **1** or **2**, wherein said antibody comprises each of the 6 CDRs as depicted in SEQ ID No: 1 for CDR-L1, SEQ ID No: 2 for CDR-L2, SEQ ID No: 3 for CDR-L3, SEQ ID No: 4 for CDR-H1, SEQ ID No: 5 for CDR-H2 and SEQ ID No: 6 for CDR-H3.

4. The use according to any one of claims **1** to **3**, wherein said antibody comprises:

- a light chain variable region (VL) as depicted in SEQ ID No: 7; and
- a heavy chain variable region (VH) as depicted in SEQ ID No: 8.

5. The use according to any one of claims **1** to **4**, wherein said antibody is selected from the group consisting of a Fv, Fab, F(ab')2, Fab', dsFv, scFv, sc(Fv)2, a diabody, and multispecific antibodies formed from antibody fragments.

6. The use according to any one of claims **1** to **5**, wherein said antibody is a monoclonal humanized antibody.

7. The use according to claim **6**, wherein:

- the heavy chain (HC) has the amino acid sequence as set forth in SEQ ID No: 9 and
- the light chain (LC) has the amino acid sequence set forth in SEQ ID No: 10.

8. The use according to any one of claims **1 to 7**, wherein said virus belongs to the MSRV subtype of human endogenous retrovirus family (HERV-W).

9. The use according to any one of claims **1 to 8**, wherein said virus is MSRV.

10. The use according to any one of claims **1 to 9**, for preventing and/or treating an HERV-W associated disease.

11. The use according to any one of claims **1 to 10**, wherein said HERV-W associated disease is selected from the group consisting of multiple sclerosis (MS), schizophrenia (SZ), bipolar disorder (BP), unipolar or psychotic depression, clinically isolated syndrome (CIS, with neurological symptom), chronic inflammatory demyelinating polyneuropathy (CIDP), epilepsy, psoriasis, cancer, inflammatory pancreatitis and diabetes such as type 1 or type 2 diabetes.

12. The use according to any one of claims **1 to 10**, wherein said HERV-W associated disease is selected from the group consisting of Multiple Sclerosis (MS) and Chronic Inflammatory Demyelinating Polyneuropathy (CIDP).

13. The use according to any one of claims **1 to 12**, wherein said retroviral reverse-transcriptase inhibitory drug is azidothymidine (AZT).

14. Use of a an antibody directed against HERV-W Envelope protein (HERV-W Env) as defined in claims **1 to 7** and a retroviral reverse-transcriptase inhibitory drug in the manufacture of a combined preparation for treating a disease selected from the group consisting of multiple sclerosis (MS), schizophrenia (SZ), bipolar disorder (BP), unipolar or psychotic depression, clinically isolated syndrome (CIS, with neurological symptom), chronic inflammatory demyelinating polyneuropathy (CIDP), epilepsy, psoriasis, cancer, inflammatory pancreatitis and diabetes such as type 1 or type 2 diabetes, wherein said combined preparation is formulated for simultaneous, separate or sequential use.

15. Use of an antibody directed against HERV-W Envelope protein (HERV-W Env) as defined in claims **1 to 7** and a retroviral reverse-transcriptase inhibitory drug in the

manufacture of a combined preparation for treating a disease selected from the group consisting of Multiple Sclerosis (MS) and Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), wherein said combined preparation is formulated for simultaneous, separate or sequential use.

16. A composition comprising:

- an antibody as defined in claims **1** to **7**; and
- a retroviral reverse-transcriptase inhibitory drug.

17. The composition according to claim **16**, wherein said retroviral reverse-transcriptase inhibitory drug is azidothymidine (AZT).