CLAIMS

1. A suppressor or inhibitor of (long interspersed element 1) LINE1 (LI) expression for use in the treatment and/or prevention of primary or secondary immunodeficiency, or of pathologies that display an immunosuppressed phenotype, preferably of cancers and/or metastasis, more preferably of lung cancer, even more preferably non-small cells lung carcinoma (NSCLC), or colorectal cancer (CRC), wherein LI comprises or consists of a sequence having 100, 99, 98, 97, 96, 95, 90, 85, 80% of identity with SEQ ID NO: 1, 2 or 3, wherein the suppressor or inhibitor is at least one molecule selected from the group consisting of:

a) a polynucleotide, selected from the group consisting of: antisense construct, antisense oligonucleotide, RNA interference construct or siRNA or a polynucleotide coding for it,

b) a vector comprising or expressing the polynucleotide as defined in a),

c) a CRISPR/Cas9 component, preferably a sgRNA, and

d) a host cell genetically engineered expressing said polypeptide or comprising the polynucleotide as defined in a) or at least one component of c).

2. The suppressor or inhibitor for use according to claim 1, wherein the treatment or prevention are performed by immunotherapy.

3. The suppressor or inhibitor for use according to claim 1 or 2, wherein the polynucleotide is an isolated inhibitory nucleic acid targeting LINE1, preferably said inhibitory nucleic acid comprises a sequence of nucleotides that are complementary to 10 to 50 consecutive nucleotides of SEQ ID NO: 1, 2 or 3.

4. The suppressor or inhibitor for use according to claim 3 wherein said inhibitory nucleic acid is at least one RNA inhibitor, preferably selected from the group consisting of: antisense oligo (ASO), gapmer, mixmer, shRNA, siRNA, stRNA, snRNA, more preferably said inhibitory nucleic acid is modified, such as 2'-deoxy-2'-fluoro- -D-arabinonucleid acid (FANA) ASO, and/or comprises one or more modified bonds or bases.

5. The suppressor or inhibitor for use according to claim 4 wherein the ASO comprises a sequence capable of hybridizing or complementary to a sequence comprising or consisting of: SEQ ID NO: 1, 2 or 3.

6. The suppressor or inhibitor for use according to anyone of claims 3-5, wherein said inhibitory nucleic acid is at least one RNA inhibitor which is an antisense oligo (ASO) comprising a nucleic acid sequence that targets one of the following sequences or the corresponding RNA sequence:

LINE1-b GGACCTCTTCAAGGAGAACTA (SEQ ID NO:5)

LINE1-c GAAGTTGAATCTCTGAATAGA (SEQ ID NO:6)

LINE1-d GGACCTCTTCAAGGAGAACTA (SEQ ID NO: 7)

LINE1-e GGAGAGGATGCGGAGAAATAG (SEQ ID NO:8),

and wherein the CRISPR/Cas9 component is a sgRNA comprising or consisting of a nucleic acid sequence that targets or is complementary to one of the following sequences:

IFNGR2-F ACTGATCGTGAGAGGCTTCGTGG (SEQ ID NO: 9)

IFNGR2-R GGTCATTTAGGGTGACAGGCAGG (SEQ ID NO: 10)

ARCP2-F GCTGTCATGGGAATCACGAAGGG (SEQ ID NO: 11)

ARCP2-R AAGGAAGACCACTTTTAAGGAGG (SEQ ID NO: 12) or to the corresponding RNA sequence.

7. The suppressor or inhibitor for use according to any one of claims 1-6, being used in T cells, B cells or Natural Killer cells.

8. The suppressor or inhibitor for use according to claim 7, wherein said T cells are selected from: CD4+ T naive cells or a CD8+ T cell, Tumor infiltrating Lymphocytes (TILs) both CD4+ and CD8+.

9. The suppressor or inhibitor for use according to claim 7 or 8, wherein said inhibitory nucleic acid is at least one RNA inhibitor which is an antisense oligo (ASO) comprising a nucleic acid sequence that targets the following sequence or the corresponding RNA sequence: LINE1-a GCACTAAATGCCTACAAGAGA (SEQ ID NO:4).

10. The suppressor or inhibitor for use according to any one of claims 1-9 in combination with an immunotherapy and/or with a radiotherapy and/or chemotherapeutic agent and/or with targeted therapies which promote raising of new antigens and immunity response and/or with immunity system adjuvants, preferably said immunotherapy comprises administration of an immune checkpoint inhibitor and/or chimeric antigen receptor (CAR)-expressing immune effector cells, preferably the immune checkpoint inhibitor is an or comprises one or more anti-CD137 antibodies; anti-PD-1 (programmed cell death 1) antibodies; anti-PDLl (programmed cell death ligand 1) antibodies; anti-PDL2 antibodies; or anti-CTLA-4 antibodies.

11. The suppressor or inhibitor for use according to any one of claims 1-10, being used in Adoptive cell transfer (ACT), cell therapy treatment, mismatched bone marrow transplantation, mismatched NK cell infusion or cytokine-induced killer (CIK) cell infusion, or wherein said suppressor or inhibitor is injected in the tumour site, e.g. in intestine tumour, melanoma, or delivered by nanoparticles specifically to the site of interest.

12. A suppressor or inhibitor of (long interspersed element 1) LINE1 (LI) expression for use in the treatment and/or prevention of a viral disease, preferably an immunodeficiency due to Human Immunodeficiency Virus (HIV) or Lymphocytic choriomeningitis virus (LCMV), wherein LI comprises or consists of a sequence having 100, 99, 98, 97, 96, 95, 90, 85, 80% of identity with SEQ ID NO: 2, or wherein LI comprises or consists of a sequence having 100, 99, 98, 97, 96, 95, 90% of identity with SEQ ID NO: 1 or 3, wherein the suppressor or inhibitor is at least one molecule selected from the group consisting of:

a) a polynucleotide, selected from the group consisting of: antisense construct, antisense oligonucleotide, RNA interference construct or siRNA or a polynucleotide coding for it,

b) a vector comprising or expressing the polynucleotide as defined in a),

c) a CRISPR/Cas9 component, preferably a sgRNA, and

d) a host cell genetically engineered expressing said polypeptide or comprising the polynucleotide as defined in a) or at least one component of c).

13. A suppressor or inhibitor of (long interspersed element 1) LINE1 (LI) expression for use as a medicament, wherein LI comprises or consists of a sequence having 100, 99, 98, 97, 96, 95, 90, 85, 80% of identity with SEQ ID NOs: 2, 5 and 9-12, wherein the suppressor or inhibitor is at least one molecule selected from the group consisting of:

a) a polynucleotide, selected from the group consisting of: antisense construct, antisense oligonucleotide, RNA interference construct or siRNA or a polynucleotide coding for it,

b) a vector comprising or expressing the polynucleotide as defined in a),

c) a CRISPR/Cas9 component, preferably a sgRNA, and

d) a host cell genetically engineered expressing said polypeptide or comprising the polynucleotide as defined in a) or at least one component of c).

14. A pharmaceutical composition comprising the suppressor or inhibitor as defined in any one of claims 1-12 and at least one pharmaceutically acceptable carrier, and optionally further comprising a therapeutic agent.

15. An in vitro method to modulate the commitment of naive CD4+ T naive cells towards any effector lineage and to modulate the effector response in dysfunctional T cells comprising the step of inhibiting LINE1 expression in said cells, wherein the step of inhibiting LINE1 expression in said cells is performed by means of at least one suppressor or inhibitor as defined in any one of claims 1-13.

16. An isolated human T cell, B cell, NK cell or Tumor cell, or a composition comprising said cell, wherein said cell is stably or transiently affected in the expression of LINE 1 (LI), wherein LI comprises or consists of a sequence having 100, 99, 98, 97, 96, 95, 90, 85, 80% of identity with SEQ ID NO: 1 or 2 or 3 preferably said cell is a CD4+ T naive cell or a CD8+ T cell, or a dysfunctional T cell, e.g. TIL.

17. The cell according to claim 15, for use as a medicament, preferably for use in the treatment and/or prevention of primary or secondary immunodeficiency, or of pathologies that display an immunosuppressed phenotype, preferably of cancers and/or metastasis, more preferably of lung cancer, even more preferably non-small cells lung carcinoma (NSCLC), or colorectal cancer (CRC), or of viral diseases such as immunodeficiencies due to HIV, Lymphocytic choriomeningitis virus (LCMV). preferably said cell or composition being used in Adoptive cell transfer (ACT), cell therapy treatment, mismatched bone marrow transplantation, mismatched NK cell infusion or cytokine-induced killer (CIK) cell infusion, or wherein said cell or composition is injected in the tumour site, preferably in intestine tumour, melanoma, or delivered by nanoparticles specifically to the site of interest.