

Claims

1. A composition comprising at least the two transcription factors : IRF8 and SPIB;
for use in reprogramming a stem cell or a differentiated cell, or mixtures thereof,
5 into a plasmacytoid dendritic cell or an interferon type I-producing cell in a
subject.
2. The composition according to claim 1, wherein the composition further
comprises one or more other transcription factors selected from the group
10 consisting of: ARID5A, BCL11A, CBFA2T3, CREB3L2, ETS1, IKZF1, STAT1,
TCF4, TCF12 and TSC22D1.
3. The composition according to any one of the previous claims, wherein the
transcription factors individually are at least 90% identical to the sequences
15 selected from the group consisting of: IRF8 (SEQ. ID. 49, SEQ. ID. 50), SPIB
(SEQ. ID. 51, SEQ. ID. 52), ARID5A (SEQ. ID. 53, SEQ. ID. 54), BCL11A
(SEQ. ID. 55, SEQ. ID. 56), CBFA2T3 (SEQ. ID. 57, SEQ. ID. 58), CREB3L2
(SEQ. ID. 59, SEQ. ID. 60), ETS1 (SEQ. ID. 61, SEQ. ID. 62), IKZF1 (SEQ. ID.
20 71, SEQ. ID. 72), TCF4 (SEQ. ID. 89, SEQ. ID. 90), TCF12 (SEQ. ID. 91, SEQ.
ID. 92), STAT1 (SEQ. ID. 93, SEQ. ID. 94) and TSC22D1 (SEQ. ID. 95, SEQ.
ID. 96).
4. The composition according to any one of the previous claims wherein the
combination of transcription factors is selected from the following combinations:
25
IRF8 and SPIB;
IRF8, SPIB and ARID5A;
IRF8, SPIB and BCL11A;
IRF8, SPIB and CBFA2T3;
30 IRF8, SPIB and CREB3L2;
IRF8, SPIB and ETS1;
IRF8, SPIB and IKZF1;
IRF8, SPIB and STAT1;
IRF8, SPIB and TCF4;
35 IRF8, SPIB and TCF12;

IRF8, SPIB and TSC22D1 or mixtures thereof.

- 5 5. The composition according to any one of the previous claims wherein the combination of transcription factors is the combination of IRF8, SPIB and TCF12.
- 10 6. The composition according to any one of the previous claims wherein the combination of transcription factors is the combination of IRF8, SPIB and TSC22D1.
- 15 7. The composition according to any one the previous claims, wherein the cell is selected from the group consisting of: pluripotent stem cell, multipotent stem cell, differentiated cell, tumor cell, cancer cell and mixtures thereof.
- 20 8. The composition according to any one of the previous claims, for use in veterinary or human medicine, in particular in the diagnosis, therapy or treatment of antiviral immune responses and immune pathology, particularly in autoimmune diseases and immunodeficiency conditions, neoplasia in particular cancer, namely solid or hematological tumors, of benign tumour, malignant tumour, early cancer, basal cell carcinoma, cervical dysplasia, soft tissue sarcoma, germ cell tumour, retinoblastoma, age-related macular degeneration, Hodgkin's lymphoma, blood cancer, prostate cancer, ovarian cancer, cervix cancer, uterus cancer, vaginal cancer, breast cancer, naso-pharynx cancer, trachea cancer, larynx cancer, bronchi cancer, bronchioles cancer, lung cancer, hollow organs cancer, esophagus cancer, stomach cancer, bile duct cancer, intestine cancer, colon cancer, colorectum cancer, rectum cancer, bladder cancer, ureter cancer, kidney cancer, liver cancer, gall bladder cancer, spleen cancer, brain cancer, lymphatic system cancer, bone cancer, pancreatic cancer, leukaemia, skin cancer, or myeloma, infectious disease, viral disease or viral induced disease, central and peripheral nervous system disorder, fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease, or viral disease, or viral induced disease, as an antiviral agent or as an immunogenic composition, immunotherapy, or in the treatment or therapy of neurodegenerative diseases, in the treatment or therapy of cancer or in the treatment or therapy of an infectious diseases, intradermal and transdermal
- 30
- 35

- therapies, HIV, infection with SARS coronavirus, Asian flu virus, herpes simplex, influenza virus, herpes zoster, hepatitis, human papillomavirus, Epstein–Barr virus, human T-lymphotropic virus or viral hepatitis, an amyloid disease in particular Amyloid A amyloidosis, Alzheimer's disease, Light-Chain (AL) amyloidosis, Type-2 Diabetes, Medullary Carcinoma of the Thyroid, Parkinson's disease, Polyneuropathy, or Spongiform Encephalopathy - Creutzfeldt Jakob disease or for drug screening.
- 5
9. A construct or a vector encoding at least the two transcription factors SPIB and IRF8.
- 10
10. The construct or vector according to claim 9, wherein the vector is a viral vector; in particular a retroviral, adenoviral, lentiviral, herpes viral, pox viral, paramyxoviral, rabdoviral, alphaviral, flaviral or adeno-associated viral vector.
- 15
11. The construct or vector according to any one of the previous claims 9 to 10, wherein the vector or construct is synthetic mRNA, naked alphavirus RNA replicons or naked flavivirus RNA replicons.
- 20
12. One or more vectors comprising at least two polynucleotide sequences encoding at least the two transcription factors IRF8 and SPIB, for use in reprogramming a stem cell or a differentiated cell, or mixtures thereof, into a plasmacytoid dendritic cell or an interferon type I-producing cell in a subject.
- 25
13. The one or more vectors of claim 12, wherein the vectors further code for one or more other transcription factors selected from the group consisting of: ARID5A, BCL11A, CBFA2T3, CREB3L2, ETS1, IKZF1, STAT1, TCF4, TCF12 and TSC22D1.
- 30
14. The one or more vectors according to any one of the previous claims 12 to 13, wherein the transcription factors individually are at least 90% identical to the sequences selected from the group consisting of: IRF8 (SEQ. ID. 1, SEQ. ID. 2), SPIB (SEQ. ID. 3, SEQ. ID. 4), ARID5A (SEQ. ID. 5, SEQ. ID. 6), BCL11A (SEQ. ID. 7, SEQ. ID. 8), CBFA2T3 (SEQ. ID. 9, SEQ. ID. 10), CREB3L2 (SEQ. ID. 11, SEQ. ID. 12), ETS1 (SEQ. ID. 13, SEQ. ID. 14), IKZF1 (SEQ. ID. 23,
- 35

SEQ. ID. 24), TCF4 (SEQ. ID. 41, SEQ. ID. 42), TCF12 (SEQ. ID. 43, SEQ. ID. 44), STAT1 (SEQ. ID. 45, SEQ. ID. 46) and TSC22D1 (SEQ. ID. 47, SEQ. ID. 48).

- 5 15. The one or more vectors according to any one of the previous claims 12 to 14, wherein the combination of transcription factors is selected from the following combinations:
- 10 IRF8 and SPIB;
 IRF8, SPIB and ARID5A;
 IRF8, SPIB and BCL11A;
 IRF8, SPIB and CBFA2T3;
 IRF8, SPIB and CREB3L2;
 IRF8, SPIB and ETS1;
15 IRF8, SPIB and IKZF1;
 IRF8, SPIB and STAT1;
 IRF8, SPIB and TCF4;
 IRF8, SPIB and TCF12;
 IRF8, SPIB and TSC22D1, or mixtures thereof.
- 20 16. The one or more vectors according to any one of the previous claims 12 to 15, wherein the combination of transcription factors is the combination of IRF8, SPIB and TCF12.
- 25 17. The one or more vectors according to any one of the previous claims 12 to 16, wherein the combination of transcription factors is the combination of IRF8, SPIB and TSC22D1.
- 30 18. The one or more vectors according to any one of the previous claims 12 to 17, wherein the vector is a viral vector; in particular a retroviral, adenoviral, lentiviral, herpes viral, pox viral, paramyxoviral, rabdoviral, alphaviral, flaviviral or adeno-associated viral vector.

19. The one or more vectors according to any one of the previous claims 12 to 18, wherein the vectors is synthetic mRNA, naked alphaviral RNA replicons or naked flavivirus RNA replicons.
- 5 20. The one or more vectors according to any one the previous claims 12 to 19, wherein the cell is selected from the group consisting of: pluripotent stem cell, multipotent stem cell, differentiated cell, tumor cell, cancer cell and mixtures thereof.
- 10 21. The one or more vectors according to any one of the previous claims 12 to 20, for use in veterinary or human medicine, in particular in the diagnosis, therapy or treatment of antiviral immune responses and immune pathology, particularly in autoimmune diseases and immunodeficiency conditions, neoplasia in particular cancer, namely solid or hematological tumors, of benign tumor, malignant tumor, early cancer, basal cell carcinoma, cervical dysplasia, soft
15 tissue sarcoma, germ cell tumor, retinoblastoma, age-related macular degeneration, Hodgkin's lymphoma, blood cancer, prostate cancer, ovarian cancer, cervix cancer, uterus cancer, vaginal cancer, breast cancer, naso-pharynx cancer, trachea cancer, larynx cancer, bronchi cancer, bronchioles
20 cancer, lung cancer, hollow organs cancer, esophagus cancer, stomach cancer, bile duct cancer, intestine cancer, colon cancer, colorectum cancer, rectum cancer, bladder cancer, ureter cancer, kidney cancer, liver cancer, gall bladder cancer, spleen cancer, brain cancer, lymphatic system cancer, bone cancer, pancreatic cancer, leukemia, skin cancer, or myeloma, infectious disease, viral
25 disease or viral induced disease, central and peripheral nervous system disorder, fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease, or viral disease, or viral induced disease, as an antiviral agent or as an immunogenic composition, immunotherapy, or in the treatment or therapy of neurodegenerative diseases, in the treatment or therapy of cancer or in the
30 treatment or therapy of an infectious diseases, intradermal and transdermal therapies, HIV, infection with SARS coronavirus, Asian flu virus, herpes simplex, influenza virus, herpes zoster, hepatitis, human papillomavirus, Epstein-Barr virus, human T-lymphotropic virus or viral hepatitis, an amyloid disease in particular Amyloid A amyloidosis, Alzheimer's disease, Light-Chain
35 (AL) amyloidosis, Type-2 Diabetes, Medullary Carcinoma of the Thyroid,

Parkinson's disease, Polyneuropathy, or Spongiform Encephalopathy -
Creutzfeldt Jakob disease or for drug screening.

- 5 22. An *in vitro* method for reprogramming or inducing a cell into a plasmacytoid
 dendritic cell or interferon type I-producing cell, comprising the following steps:
- transducing a cell selected from the group consisting of: a stem cell, a
 differentiated cell, and mixtures thereof,
 with one or more vectors comprising at least the two transcription factors
10 selected from the group consisting of: IRF8 and SPIB.
23. The method according to claim 22, wherein the one or more vectors further
 comprise one or more transcription factors selected from the group consisting
 of: ARID5A, BCL11A, CBFA2T3, CREB3L2, ETS1, IKZF1, STAT1, TCF4,
15 TCF12 and TSC22D1.
24. The method according to any one of the previous claims 22 to 23, wherein the
 transcription factors individually are at least 90% identical to the sequences
 selected from the group consisting of: : IRF8 (SEQ. ID. 1, SEQ. ID. 2), SPIB
20 (SEQ. ID. 3, SEQ. ID. 4), ARID5A (SEQ. ID. 5, SEQ. ID. 6), BCL11A (SEQ. ID.
 7, SEQ. ID. 8), CBFA2T3 (SEQ. ID. 9, SEQ. ID. 10), CREB3L2 (SEQ. ID. 11,
 SEQ. ID. 12), ETS1 (SEQ. ID. 13, SEQ. ID. 14), IKZF1 (SEQ. ID. 23, SEQ. ID.
 24), TCF4 (SEQ. ID. 41, SEQ. ID. 42), TCF12 (SEQ. ID. 43, SEQ. ID. 44),
 STAT1 (SEQ. ID. 45, SEQ. ID. 46) and TSC22D1 (SEQ. ID. 47, SEQ. ID. 48).
25
25. The method according to any one of the previous claims 22 to 24, wherein the
 combination of transcription factors is selected from the following combinations:
- IRF8 and SPIB;
30 IRF8, SPIB and ARID5A;
 IRF8, SPIB and BCL11A;
 IRF8, SPIB and CBFA2T3;
 IRF8, SPIB and CREB3L2;
 IRF8, SPIB and ETS1;
35 IRF8, SPIB and IKZF1;

IRF8, SPIB and STAT1;
IRF8, SPIB and TCF4;
IRF8, SPIB and TCF12;
IRF8, SPIB and TSC22D1, or mixtures thereof.

5

26. The method according to any one of the previous claims 22 to 25, culturing the transduced cells during at least 2 days, preferably at least 5 days, more preferably at least 8 days, even more preferably at least 9 days.

10

27. The method according to any one of the previous claims 22 to 26, wherein the transducing step further comprises at least one vector selected from the group consisting of: a nucleic acid sequence encoding IL-12; nucleic acid sequence encoding IL-4; a nucleic acid sequence encoding IFN- α ; a nucleic acid sequence encoding IFN- β ; a nucleic acid sequence encoding IFN- γ ; a nucleic acid sequence encoding TNF; nucleic acid sequence encoding GM-CSF; nucleic acid sequence encoding siRNAs targeting IL-10 RNA, and mixtures thereof, preferably comprising nucleic acids encoding immunostimulatory cytokines.

15

20

28. The method according to any one of the previous claims 22 to 27, wherein the cell is a mammalian cell, a human cell, a non-human cell or a mouse cell selected from the group consisting of: of pluripotent stem cell, or multipotent stem cell, differentiated cell, wherein the pluripotent stem cell, multipotent stem cell, or differentiated cell, is selected from the group consisting of: an endoderm derived cell, a mesoderm derived cell, or an ectoderm derived cell, a multipotent stem cell including mesenchymal stem cell, a hematopoietic stem cell, an intestinal stem cell, a pluripotent stem cell and a cell line; in particular a mesoderm-derived cell preferably a monocyte and mixtures thereof.

25

30

29. An induced plasmacytoid dendritic cell or interferon type I-producing cell obtained by the method described in any of the claims 22 to 28.

35

30. A composition comprising a plasmacytoid dendritic cell or an interferon type I-producing cell according to claim 29 in a therapeutically effective amount further comprising a pharmaceutically acceptable excipient, an analgesic, an anti-

inflammatory agent, a chemotherapy agent, a radiotherapy agent, an antibiotic, a diuretic, a filler, a binder, a disintegrant, or a lubricant, or mixtures thereof.

5 31. A vaccine or an injectable formulation, in particular an in-situ injection comprising the composition according to any one of claims 1 to 8 and 30, and/or the induced plasmacytoid dendritic cell or interferon type I-producing cell according to claim 29, or mixtures thereof.

10 32. A kit comprising at least one of the following components:
the induced plasmacytoid dendritic cell or interferon type I -producing cell according to claim 29;
the composition according to any of claims 1 to 8 and 30;
the vector or a construct according to claims 9 to 21 ; or mixtures thereof.

15