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, into a plasmacytoid dendritic 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 consisting of: ARID5A, BCL11A, CBFA2T3, CREB3L2, ETS1, IKZF1, IKZF2, 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 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. 71, SEQ. ID. 72), IKZF2 (SEQ ID NO. 73, SEQ ID NO. 74), 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 composition comprises the combination of transcription factors is selected from the following combinations:

    IRF8 and SPIB;
    IRF8, SPIB and ARID5A;
    IRF8, SPIB and BCL11A;
    IRF8, SPIB and CBFA2T3;
    IRF8, SPIB and CREB3L2;
    IRF8, SPIB and ETS1;
    IRF8, SPIB and IKZF1;
    IRF8, SPIB and IKZF2;
    IRF8, SPIB and STAT1;

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

5. The composition according to claim 4 wherein the combination of transcription factors is the combination of IRF8, SPIB and TCF12.

6. The composition according to claim 4 wherein the combination of transcription factors is the combination of IRF8, SPIB and TSC22D1.

7. The composition according to claim 4, wherein the combination of transcription factors is the combination of IRF8, SPIB and IKZF2.

8. The composition according to any one the previous claims, wherein the stem cell or the differentiated cell, or mixtures thereof is selected from the group consisting of: pluripotent stem cell, multipotent stem cell, differentiated cell, tumor cell, cancer cell and mixtures thereof.

9. Use of the composition according to any one of the previous claims, for the manufacturing of a medicament.

10. The use according to claim 9, wherein the medicament is for treating cancer, autoimmune diseases, cancer or infectious diseases.

11. A construct or a vector encoding at least the two transcription factors SPIB and IRF8.

12. The construct or vector according to claim 11, 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.

13. The construct or vector according to any one of the previous claims 11 to 12, wherein the vector or construct is synthetic mRNA, naked alphavirus RNA replicons or naked flavivirus RNA replicons.

14. A composition comprising one or more vectors comprising at least two polynucleotide sequences, which vectors in combination encode 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 in a subject.

15. The composition according to claim 14, wherein the vectors further code for one or more other transcription factors selected from the group consisting of: ARID5A, BCL11A, CBFA2T3, CREB3L2, ETS1, IKZF1, IKZF2, STAT1, TCF4, TCF12 and TSC22D1.

16. The composition according to any one of the previous claims 14 to 15, 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, SEQ. ID. 24), IKZF2 (SEQ ID NO. 25, SEQ ID NO. 26), 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).

17. The composition according to any one of the previous claims 14 to 16, wherein the combination of transcription factors is selected from the following combinations:

IRF8 and SPIB;
IRF8, SPIB and ARID5A;
IRF8, SPIB and BCL11A;
IRF8, SPIB and CBFA2T3;
IRF8, SPIB and CREB3L2;
IRF8, SPIB and ETS1;
IRF8, SPIB and IKZF1;
IRF8. SPIB and IKZF2;
IRF8, SPIB and STAT1;
IRF8, SPIB and TCF4;
IRF8, SPIB and TCF12;
IRF8, SPIB and TSC22D1, or mixtures thereof.

18. The composition according to claim 17, wherein the combination of transcription factors is the combination of IRF8, SPIB and TCF12.

19. The composition according to claim 17, wherein the combination of transcription factors is the combination of IRF8, SPIB and TSC22D1.

20. The composition according to claim 17, wherein the combination of transcription factors is the combination of IRF8, SPIB and IKZF2.

21. The composition according to any one of the previous claims 14 to 20, 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.

22. The composition according to any one of the previous claims 14 to 21, wherein the vectors is synthetic mRNA, naked alphaviral RNA replicons or naked flavivirus RNA replicons.

23. The composition according to any one the previous claims 14 to 22, wherein the stem cell or the differentiated cell, or mixtures thereof is selected from the group consisting of: pluripotent stem cell, multipotent stem cell, differentiated cell, tumor cell, cancer cell and mixtures thereof.

24. Use of the composition according to any one of the previous claims 14 to 23, for the manufacturing of a medicament.

25. The use according to claim 24, wherein the medicament is for treating cancer, autoimmune diseases, or infectious diseases.

26. An *in vitro* method for reprogramming or inducing a cell into a plasmacytoid dendritic 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 selected from the group consisting of: IRF8 and SPIB.

27. The method according to claim 26, 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, IKZF2, STAT1, TCF4, TCF12 and TSC22D1.

28. The method according to any one of the previous claims 26 to 27, 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, SEQ. ID. 24), IKZF2 (SEQ ID. 25, SEQ ID. 26), 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).

29. The method according to any one of the previous claims 26 to 28, wherein the one or more vectors comprise the combination of transcription factors is selected from the following combinations:

IRF8 and SPIB;
IRF8, SPIB and ARID5A;
IRF8, SPIB and BCL11A;
IRF8, SPIB and CBFA2T3;
IRF8, SPIB and CREB3L2;
IRF8, SPIB and ETS1;
IRF8, SPIB and IKZF1;
IRF8, SPIB and IKZF2;
IRF8, SPIB and STAT1;
IRF8, SPIB and TCF4;
IRF8, SPIB and TCF12;
IRF8, SPIB and TSC22D1, or mixtures thereof.

30. The method according to any one of the previous claims 26 to 29, 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.

31. The method according to any one of the previous claims 26 to 30, 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-a; a nucleic acid sequence encoding IFN-f3; a nucleic acid sequence encoding IFN-y; 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.

32. The method according to any one of the previous claims 26 to 31, 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.