

CLAIMS:

1. Use of non-coding RNA expression data or expression profiles of a cell population to identify, determine or infer the propensity of that cell population for a cellular functional effect for a pre-determined purpose, which cellular functional effect is a functional effect of a cell population which effect is temporally, procedurally or interventionally separated from the cell population from which the expression data or expression profiles derive.
2. A use as claimed in claim 1, wherein the cellular functional effect may be demonstrable a period of time after an assay for identifying, determining or inferring the cellular functional effect.
3. A use as claimed in claim 1, wherein the cellular functional effect may be demonstrable upon a process or procedure being applied to the cell population from which the non-coding RNA expression data or expression profiles derive.
4. A use as claimed in claim 1, wherein the cellular functional effect may be demonstrable after an intervention is performed on the cell population from which the non-coding RNA expression data or expression profiles derive.
5. A use as claimed in any one of claims 1 to 3, wherein the non-coding RNA expression data is of a pre-determined non-coding RNA or panel of non-coding RNA the expression of which is known to correlate with the cellular functional effect or a known surrogate or assay thereof.
6. A use as claimed in claim 5, which can be effected by assaying against the pre-determined non-coding RNA or panel of non-coding RNA.
7. A use as claimed in claim 5, wherein the panel of non-coding RNA comprises at least two non-coding RNA and preferably up to six non-coding RNA.

8. A use as claimed in claim 7, wherein at least one non-coding RNA is positively correlated and at least one non-coding RNA is negatively correlated with the cellular functional effect.

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9. A use as claimed in any one of the preceding claims wherein the pre-determined purpose is selected from a bioprocess applications, a cell therapy application, patient stratification for cell therapy, cell growth and donor selection.

10 10. A use as claimed in any one of the preceding claims, wherein the cellular functional effect is an effect on an applied cell population by a tissue to which it is applied, an effect on a tissue to which a cell population is applied, production of paracrine factors, proliferation activity, differentiation tendency, engraftment potential, immunosuppressive activity, migration potential, response to activity
15 inducing agents or response to assays.

11. A use as claimed in any one of the preceding claims which is further for making a selection or treatment decision based upon the identification, determination or inference of propensity for the cellular functional effect.

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12. A method of inferring propensity of a cell population for a cellular functional effect for a pre-determined purpose, the method comprising assaying the cell population against a pre-determined non-coding RNA or panel of non-coding RNAs known or determined to correlate with the cellular functional effect,
25 generating non-coding RNA expression data for the assayed non-coding RNA or panel of non-coding RNAs and from the non-coding RNA expression data identifying, determining or inferring a propensity for the cellular functional effect, wherein the cellular functional effect is a functional effect of a cell population which effect is temporally, procedurally or interventionally separated from the cell
30 population from which the expression data or expression profiles derive. .

13. A method as claimed in claim 12, wherein the identifying, determining or inferring a propensity for the cellular functional effect is by comparing the expression data from the assay with expression levels, trends or patterns known to be associated with cellular functional effect.
- 5 14. A method as claimed in claim 12 or claim 13, which is for inferring a cellular functional effect in a cell population by assaying that cell population against the predetermined non-coding RNA or panel of non-coding RNAs.
- 10 15. A method as claimed in any one of claims 12 to 14, wherein the panel of non-coding RNA comprises at least two non-coding RNA and preferably up to six non-coding RNA.
- 15 16. A method as claimed in claim 15, wherein at least one non-coding RNA is positively correlated and at least one non-coding RNA is negatively correlated with the cellular functional effect.
- 20 17. A method as claimed in any one of claims 12 to 16, wherein the predetermined purpose is selected from a bioprocess applications, a cell therapy application, patient stratification for cell therapy, cell growth and donor selection.
- 25 18. A method as claimed in any one of claims 12 to 17, wherein the cellular functional effect is an effect on an applied cell population by a tissue to which it is applied, an effect on a tissue to which a cell population is applied, production of paracrine factors, proliferation activity, differentiation tendency, engraftment potential, immunosuppressive activity, migration potential, response to activity inducing agents or response to assays.
- 30 19. A method as claimed in any one of claims 12 to 18, which further comprises making a selection or treatment decision based upon the identification, determination or inference of propensity for the cellular functional effect.

20. A use or method as claimed in any one of the preceding claims, which is for inferring a cellular functional effect in a cell population using the non-coding RNA expression data from that cell population for a predetermined non-coding RNA or panel of non-coding RNAs, wherein the cell population are human cells.
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21. A use or method as claimed in claim 20, wherein the cells are stem cells or T-cells.
22. A use or method as claimed in claim 21, wherein the cells are T-cells
- 10 which are optionally modified for surface antigenic activity.
23. A use or method as claimed in claim 22, wherein the cellular functional effect comprises migratory potential of the T-cells to target tumour cells and the pre-determined purpose is the treatment of a cancer.
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24. A use or method as claimed in claim 21, wherein the cells are stem cells.
25. A use or method as claimed in claim 24, which cells are stem cells selected from MSCs, induced pluripotent stem cells or haematopoietic stem cells such as
- 20 CD34+ cells.
26. A use or method as claimed in claim 25, wherein the cells are MSCs.
27. A use or method as claimed in claim 25 or claim 26, wherein the cellular
- 25 functional effect is differentiation into chondrocytes and the pre-determined purpose is regenerative treatment of cartilage tissue.
28. A use or method as claimed in claim 25 or claim 26, wherein the cellular
- 30 functional effect is differentiation into osteocytes and the pre-determined purpose is regenerative treatment of bone tissue.

29. A use or method as claimed in claim 25 or claim 26, wherein the cellular functional effect is secretion of paracrine factors and the pre-determined purpose is regenerative treatment of target tissue.
- 5 30. A use or method as claimed in claim 29, wherein the cellular functional effect is secretion of one or more paracrine factors known to influence a pre-determined target tissue regeneration and the pre-determined purpose is regenerative treatment of target tissue.
- 10 31. A use or method as claimed in claim 30, wherein the paracrine factors are growth factors for one of vascular smooth muscle and/or cardiomyocytes and the pre-determined purpose is regenerative treatment of cardiac or vascular tissue.
- 15 32. A use or method as claimed in claim 26, wherein the cellular functional effect is the IDO induction of the MSCs by interferon-gamma and the pre-determined purpose is treatment of T-cell proliferation-mediated indications or Graft vs Host Disease.
- 20 33. A use or method as claimed in claim 25, wherein the cellular functional effect is migration toward stromal cell-derived-factor 1 (SDF-1) and the pre-determined purpose is selection of donors of stem cells for engraftment potential.
- 25 34. A use or method as claimed in claim 33, wherein the stem cells are CD34+ cells.
- 30 35. A use or method as claimed in claim 20, wherein the pre-determined purpose is for the treatment of one of an immune disorder such as Crohn's disease, rheumatoid arthritis, lupus, IBD or MS, a cancer, a cardiovascular disease or a tissue-degenerative disorder.
36. A method of applying a cell population to a pre-determined purpose, the method comprising inferring a cellular function effect for the predetermined

purpose by the method of any one of claims 12 to 35 and applying the cell population for the pre-determined purpose.

37. A method for screening populations of donor-derived cells (e.g. stem cells
5 such as MSCs) for use in treatment of an indication or condition or for further manipulation for later treatment of an indication or conditions, the method comprising inferring a cellular function effect pertinent to the treatment of the indication or the further manipulation and in dependence of that inference, selecting populations of donor-derived cells (or selecting donors for further
10 donation of cells) for use in the treatment of the indication or the further manipulation.

38. A method for determining the dose of a population of cells (e.g stem cells, such as MSCs or T-cells) for administration to a patient for treating a condition
15 which depends upon a cellular functional effect, the method comprising measuring an non-coding RNA expression profile for the cells for a pre-determined non-coding RNA or panel of non-coding RNAs known to correlate with the cellular functional effect and inferring therefrom a relative propensity to the cellular functional effect and determining therefrom with reference to a predetermined
20 dose for a pre-determined propensity to the cellular functional effect an actual dose to be administered to a patient.

39. A method of treatment of a human or animal patient in need thereof, the method comprising administering one or a plurality of cell therapy doses to said
25 patient, said cell therapy dose effective in treating said patient by a cellular function effect as between the cell therapy and the patient, the cellular function effect having been inferred by use of non-coding RNA expression profile.

40. A method as claimed in claim 38 or claim 39, wherein the treatment is one
30 of autologous cell therapy or allogenic cell therapy.

41. A population of cells selected to have a non-coding RNA expression profile for a pre-defined non-coding RNA or panel of non-coding RNAs that correlates with a pre-defined cellular functional effect optionally for a pre-determined purpose, which cellular functional effect is a functional effect of a cell population which effect is temporally, procedurally or interventionally separated from the cell population from which the expression data or expression profiles derive.
42. A population of cells as claimed in claim 41, derived from a donor of said cells, the donor having been selected based upon a non-coding RNA expression profile for a pre-defined non-coding RNA or panel of non-coding RNAs that correlates with a pre-defined cellular functional effect.
43. A cell population as claimed in claim 41 or claim 42 for use in therapy or diagnosis of the human or animal body.
44. A cell population for use in the treatment of a condition in a patient in need thereof, which treatment is mediated by a pre-defined cellular functional effect, the cell population provided in a dose or dosage regimen determined according to the non-coding RNA expression of the cell population for a pre-defined non-coding RNA or panel of non-coding RNAs that correlates with the cellular functional effect to a degree that corresponds with one of a plurality of possible doses or dosage regimen.
45. A cell population as claimed in any one of claims which are human cells.
46. A cell population as claimed in claim 44 or claim 45 which cells are stem cells or T-cells.
47. A cell population as claimed in claim 46, wherein the cells are T-cells which are optionally modified for surface antigenic activity.

48. A cell population as claimed in claim 45, for the treatment of a cancer.
49. A cell population as claimed in claim 46, wherein the cells are stem cells.
- 5 50. A cell population as claimed in claim 46, which cells are stem cells selected from MSCs, induced pluripotent stem cells or haematopoietic stem cells such as CD34+ cells.
- 10 51. A cell population as claimed in claim 50, wherein the stem cells are MSCs.
52. A cell population as claimed in any one of claims 49 to 51, wherein the cellular functional effect is differentiation into chondrocytes and the pre-determined purpose is regenerative treatment of cartilage tissue.
- 15 53. A cell population as claimed in any one of claims 49 to 51, wherein the cellular functional effect is differentiation into osteocytes and the pre-determined purpose is regenerative treatment of bone tissue.
- 20 54. A cell population as claimed in any one of claims 49 to 51, wherein the cellular functional effect is secretion of paracrine factors and the pre-determined purpose is regenerative treatment of target tissue.
- 25 55. A cell population as claimed in claim 54, wherein the cellular functional effect is secretion of one or more paracrine factors known to influence a pre-determined target tissue regeneration and the pre-determined purpose is regenerative treatment of target tissue.
- 30 56. A cell population as claimed in claim 54, wherein the paracrine factors are growth factors for one of vascular smooth muscle and/or cardiomyocytes and the pre-determined purpose is regenerative treatment of cardiac or vascular tissue.

57. A cell population as claimed in claim 51, wherein the cellular functional effect is the IDO induction of the MSCs by interferon-gamma and the pre-determined purpose is treatment of T-cell proliferation-mediated indications or Graft vs Host Disease.

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58. A cell population as claimed in claim 49 or claim 50 wherein the cellular functional effect is migration toward stromal cell-derived-factor 1 (SDF-1) and the pre-determined purpose is selection of donors of stem cells for engraftment potential.

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59. A cell population as claimed in claim 58, wherein the stem cells are CD34+ cells.

60. A cell population as claimed in any one of claims 41 to 44, which is for the treatment of one of an immune disorder such as Crohn's disease, rheumatoid arthritis, lupus, IBD or MS, a cancer, a cardiovascular disease or a tissue-degenerative disorder.

61. A kit for use to identify, determine or infer the propensity or relative propensity of a population of cells for a cellular functional effect, optionally for use in a pre-determine purpose, the kit comprising primers for use in quantitative PCR (polymerase chain reaction), primers being for a non-coding RNA or panel of non-coding RNAs known or identified as correlating with the cellular functional effect, which cellular functional effect is a functional effect of a cell population which effect is temporally, procedurally or interventionally separated from the cell population from which the expression data or expression profiles derive. .

62. A kit as claimed in claim 61, which further comprises a protocol and methods for the PCR assay.

63. A method of identifying or determining one or more non-coding RNA the expression of which in the cell population being assayed is correlating with a cellular functional effect of the cell population (e.g. when administered, subject to an intervention or treated), which cellular functional effect is a functional effect of a cell population which effect is temporally, procedurally or interventionally separated from the cell population from which the expression data or expression profiles derive, preferably for a predetermined purpose, for use of said one or more non-coding RNAs in a panel for identifying, determining or inferring the cellular functional effect, the method comprising:
- 10 - Sourcing cell populations intended for effecting the cellular functional effect from multiple sources (e.g. multiple donors or multiple production batches of different provenance);
 - Treating and using a first sample of each cell population to isolate total RNA for non-coding RNA expression profiling thereby generating an
15 extensive (e.g. based on at least 100 miRNAs, preferably at least 800, more preferably at least 1000 and most preferably at least 2000 miRNAs) non-coding RNA expression profile data set for each cell population;
 - Subjecting a second sample of each cell population to an intervention designed to elicit a cellular functional effect and the extent of the cellular
20 functional effect monitored by a known or conventional or surrogate means to generate 'response data';
 - Correlating the extensive non-coding RNA expression profile data set with response data for each cell population;
 - Identifying correlating non-coding RNA, preferably that correlate
25 positively or negatively with a correlation coefficient of at least 7 or at least 8; and
 - selecting such correlating non-coding RNA as candidates for a non-coding RNA expression panel for the cellular functional effect.
- 30 64. A use, methods, population of cells or kit as claimed in any one of the preceding claims, wherein the non-coding RNA are miRNA.