

~~I/We Claim~~ **CLAIMS:**

1. An *in-vitro* method for detecting a medical condition in a subject, said method comprising:

~~a)~~ ~~obtaining a sample;~~

b)a) enriching very small embryonic like stem cells from the blood sample, to obtain a mixture comprising said very small embryonic like stem cells;

~~e)b)~~ obtaining nucleic acid from the mixture of step (b)a);

~~d)c)~~ performing an assay with the nucleic acid for analysing expression level of Oct4A in the very small embryonic like stem cells from the blood sample; and

~~e)d)~~ comparing the expression level of Oct4A in the very small embryonic like stem cells from the blood sample with an expression level of Oct4A in a control sample,

wherein an increase in the range of 1.1-3 folds in the expression level of Oct4A in the very small embryonic like stem cells from the blood sample as compared to the expression level of Oct4A in the control sample detects an inflammatory status indicative of the presence of a medical condition in the subject, wherein the method is an *in-vitro* method, and wherein the medical condition is selected from the group consisting of multiple sclerosis, kidney disorders, skin disease, liver disease, lung disease, cardiovascular diseases, osteoarthritis, viral disease, and diabetes.

2. An *in-vitro* method for predicting onset of cancer in a subject, said method comprising:

~~a)~~ ~~obtaining a sample;~~

b)a) _____ enriching very small embryonic like stem cells from ~~the~~ blood sample, to obtain a mixture comprising said very small embryonic like stem cells;

e)b) _____ obtaining nucleic acid from the mixture of step (b)a);

d)c) _____ performing an assay with the nucleic acid for analysing expression level of Oct4A in the very small embryonic like stem cells; and

e)d) _____ comparing the expression level of Oct4A in the very small embryonic like stem cells from the blood sample with an expression level of Oct4A in a control sample,

wherein an increase in the range of 3-5 folds in the expression level of Oct4A in the very small embryonic like stem cells from the blood sample as compared to the expression level of Oct4A in the control sample predicts the onset of cancer in the subject, and wherein the method is an *in-vitro* method.

3. An *in-vitro* method for detecting the presence of cancer in a subject, said method comprising:

a) ~~obtaining a sample;~~

b)a) _____ enriching very small embryonic like stem cells from ~~the~~ a blood sample, to obtain a mixture comprising said very small embryonic like stem cells;

e)b) _____ obtaining nucleic acid from the mixture of step (b)a);

d)c) _____ performing an assay with the nucleic acid for analysing expression level of Oct4A in the very small embryonic like stem cells; and

e)d) _____ comparing the expression level of Oct4A in the very small embryonic like stem cells from the blood sample with an expression level of Oct4A in a control sample,

wherein an increase of at least 5 folds in the expression level of Oct4A in the very small embryonic like stem cells from the blood sample as compared to the

expression level of Oct4A in the control sample detects the presence of cancer in the subject, and wherein the method is an *in-vitro* method.

4. The method as claimed in any one of the claims 1-3, wherein the method further comprises analysing the nucleic acid by performing sequence-based assays.

5. The method as claimed in any one of the claims 2- or 3, wherein analysing the nucleic acid by sequence-based assays detects the type of cancer.

6. The method as claimed in claim 3, wherein the increase in the expression level of Oct4A in the very small embryonic like stem cells from the sample is in the range of 5-10, 10-15 folds, 15-20 folds, or 20-25 folds as compared to the expression level of Oct4A in the control.

~~7. The method as claimed in claim 3, wherein the increase in the expression level of Oct4A in the very small embryonic like stem cells from the sample is in the range of 10-15 folds as compared to the expression level of Oct4A in the control.~~

~~8. The method as claimed in claim 3, wherein the increase in the expression level of Oct4A in the very small embryonic like stem cells from the sample is in the range of 15-20 folds as compared to the expression level of Oct4A in the control.~~

~~9. The method as claimed in claim 3, wherein the increase in the expression level of Oct4A in the very small embryonic like stem cells from the sample is in the range of 20-25 folds as compared to the expression level of Oct4A in the control.~~

~~10-7.~~ An *in-vitro* method for monitoring response to anti-cancer therapy, said method comprising:

~~a) obtaining a sample at one time point during an anti-cancer therapy;~~

~~b)~~ a) enriching very small embryonic like stem cells from the a blood sample from one time point during an anti-cancer therapy to obtain a mixture comprising said very small embryonic like stem cells;

~~c)~~ b) obtaining nucleic acid from the mixture of step (b);

~~d)c)~~_____performing an assay with the nucleic acid for analysing expression level of Oct4A in the very small embryonic like stem cells from the blood sample; and

~~e)d)~~_____comparing the expression level of Oct4A in the very small embryonic like stem cells from the blood sample with an expression level of Oct4A in very small embryonic like stem cells in a reference that monitors the response to anti-cancer therapy, , and wherein the method is an *in-vitro* method.

~~11.8.~~_____The method as claimed in claim ~~107~~, wherein the reference is at least one selected from a group consisting of: (a) a blood sample obtained prior to administration of anti-cancer therapy; (b) a blood sample obtained at a previous time point as compared to the time point mentioned in step (a) of claim ~~107~~; (c) a blood sample obtained at a subsequent time point as compared to the time point mentioned in step (a) of claim ~~107~~; and (d) a blood sample obtained from a cancer-free subject.

~~12.9.~~_____The method as claimed in claim ~~107~~, wherein a decrease in the expression level of Oct4A in very small embryonic like stem cells in the blood sample as compared to the expression level in the reference indicates a positive response to the anti-cancer therapy, and wherein the reference is at least one selected from the group consisting of: (a) a blood sample obtained prior to administration of anti-cancer therapy; (b) a blood sample obtained at a previous time point as compared to the time point mentioned in step (a) of claim ~~107~~; and (c) a blood sample obtained from a cancer-free subject.

~~13.10.~~_____ An *in-vitro* method for detecting a positive response to anti-cancer therapy, said method comprising:

- ~~a)~~_____obtaining a sample I before administration of an anti-cancer therapy;
- ~~b)~~_____obtaining a sample II after administration of the anti-cancer therapy;

e)a) _____enriching very small embryonic like stem cells from ~~the~~a blood
sample-I from before administration of an anti-cancer therapy to obtain a
mixture-I comprising said very small embryonic like stem cells;

d)b) _____enriching very small embryonic like stem cells from ~~the~~a blood
sample-II from after administration of the anti-cancer therapy to obtain a
mixture-II comprising said very small embryonic like stem cells;

e)c) _____obtaining nucleic acid-I from the mixture-I;

f)d)obtaining nucleic acid-II from the mixture-II;

g)e) _____independently performing an assay with the nucleic acid-I and the
nucleic acid-II for analysing expression level of Oct4A; and

h)f)comparing the expression levels of Oct4A from the nucleic acid-II with the
expression level of Oct4A from the nucleic acid-I,

wherein a decrease in the expression level of Oct4A from the nucleic acid-II
as compared to the expression level of Oct4A from the nucleic acid-I detects a
positive response to the cancer treatment, and wherein the method is an *in-vitro*
method.

14. — ~~An *in-vitro* method for detecting cancer, said method comprising:~~

~~e) obtaining a sample;~~

~~p) enriching very small embryonic like stem cells from the sample, to obtain a
mixture comprising said very small embryonic like stem cells;~~

~~q) obtaining nucleic acid from the mixture of step (b);~~

~~r) performing an assay with the nucleic acid for analysing expression level of
Oct4A in very small embryonic like stem cells;~~

~~s) comparing the expression level of Oct4A in very small embryonic like stem
cells in the sample with an expression level of Oct4A in very small
embryonic like stem cells in a control sample, wherein an increase in the
expression level of Oct4A in very small embryonic like stem cells in the
sample as compared to the expression level of Oct4A in very small~~

embryonic like stem cells in the control sample indicates presence of cancer;
and

t) ~~performing sequence based assays on the nucleic acid and analysing for
mutation in at least one cancer related marker,
wherein presence of mutation in the at least one cancer related marker
indicates presence of a specific type of cancer based on the cancer related
marker analysed.~~

~~22.11.~~ The method as claimed in any one of the claims 1-3, ~~10, 13, or 14~~, or 10,
wherein obtaining the nucleic acid from the mixture is by any one method selected
from a group consisting of: (a) guanidinium thiocyanate-phenol-chloroform nucleic
acid extraction; (b) cesium chloride gradient centrifugation method; (c)
cetyltrimethylammonium bromide nucleic acid extraction; (d) alkaline extraction;
(e) resin-based extraction; and (f) solid phase nucleic acid extraction.

~~23.12.~~ The method as claimed in any one of the claims 1-3, ~~10, 13, or 14~~ or 10,
wherein performing an assay with the nucleic acid for analysing the expression of
Oct4A is done by a technique selected from a group consisting of quantitative PCR,
flow cytometry, and Next Generation Sequencing (NGS).

~~24.13.~~ The method as claimed in any one of the claims 1-3, ~~or 14~~, wherein the
control is the expression level of Oct4A in very small embryonic like stem cells
obtained from a healthy subject or a cancer-free subject.

~~25.14.~~ The method as claimed in any one of the claims 1-3, 7 or 10, ~~13, or 14~~,
wherein the enriching of the very small embryonic like stem cells from a blood
sample comprises:

- a) contacting the blood sample with a neutral buffer in a ratio range of 1:1 to
1:20, to obtain a first mixture;
- b) centrifuging the first mixture, to obtain a second mixture comprising red
blood cells (RBC) fraction; and

- c) processing the second mixture to obtain enriched very small embryonic like stem cells.

26-15. The method as claimed in claim 14, wherein the processing of the second mixture comprising RBC fraction, comprises at least one method selected from a group consisting of: (a) extraction process comprising lysis of the RBC fraction; (b) washing process; (c) centrifugation process, and combinations thereof.

~~27. The method as claimed in claim 14, wherein the cancer-related marker is selected from a group consisting of well known markers established to be related to cancer.~~

~~28. The method as claimed in any one of the claims 1-3, 10, 13, or 14, wherein the method is independent of invasive techniques.~~

~~29. A method for treating cancer, said method comprising:~~

~~dd) obtaining a sample from a subject;~~

~~ee) enriching very small embryonic like stem cells from the sample, to obtain a mixture comprising said very small embryonic like stem cells;~~

~~ff) obtaining nucleic acid from the mixture of step (b);~~

~~gg) performing an assay with the nucleic acid for analysing expression level of Oct4A in very small embryonic like stem cells;~~

~~hh) comparing the expression level of Oct4A in very small embryonic like stem cells in the sample with an expression level of Oct4A in a control sample;~~

~~wherein an increase in the expression level of Oct4A in very small embryonic like stem cells in the sample as compared to the expression level of Oct4A in the control sample detects cancer; and~~

~~ii) administering anti-cancer therapy to the subject for treating cancer.~~

36-16. The method as claimed in claim 3, wherein the increase in the expression level of Oct4A in the very small embryonic like stem cells from the blood sample in the range of 5-10 folds as compared to the expression level of Oct4A in the control indicates stage I of cancer, in the range of 10-15 folds as compared to the expression level of Oct4A in the control indicates stage II of cancer, and in the range of 15-20

folds as compared to the expression level of Oct4A in the control indicates stage III of cancer.

37. ~~The method as claimed in claim 3, wherein the increase in the expression level of Oct4A in the very small embryonic like stem cells from the sample in the range of 10-15 folds as compared to the expression level of Oct4A in the control indicates stage II of cancer.~~

38. ~~The method as claimed in claim 3, wherein the increase in the expression level of Oct4A in the very small embryonic like stem cells from the sample in the range of 15-20 folds as compared to the expression level of Oct4A in the control indicates stage III of cancer.~~

39. ~~17. _____~~ The method as claimed in claim 3, wherein the increase in the expression level of Oct4A in the very small embryonic like stem cells from the blood sample in the range of 20 and higher folds as compared to the expression level of Oct4A in the control indicates stage IV of cancer.

40. ~~The method as claimed in claim 14, wherein the cancer-related marker is selected from the group consisting of mir145, OLR1, CD68, MSR1, CXCL16, NCAN, TKTL1, ANO4, CHIT1, GPNMB, CCL18, TGFbeta1, FSP1, S100A6, SLC13A3, BGN, NCF2, 6Ckine, MMP 9, MMP 3, MMP 7, Integrin beta4, Pleiotrophin, urokinase R, HLA-C, SLC9A3R1, NAT9, RAPTOR and SLC12A8, SPINK5, FcepsilonRI beta, PHF11, IGFBP1, FACI4, IL1R, TGFbeta, CHRNA3/5, IREB2, HHIP, FAM13A, AGER, Troponin T&I, HSP60, BNP, GDF-15, MMP2, MMP3, MMP9, IL6, TNFalpha, CRP, SOX9, ACAN, COL2A1, DKK1, FRZB, RUNX2, COL10A1, IGH, IGHM, IGHG1, Sirtuins, ACE2, IFI27, IFIT1, IFITM1, DPP4, KRAS, BRCA1 and 2, TP53, HLA-DQA1, HLA-DQB1, HLA-DRB1 (Type I), PPARG, KCNJ11, CDKAL1, CDKN2A-CDKN2B, IDE-KIF11-HHEX, IGF2BP2 and SLC30A8 (Type II), and combinations thereof.~~

41. ~~The method as claimed in claim 1, wherein the medical condition identified is selected from the group consisting of multiple sclerosis, kidney disorders, skin~~

disease, liver disease, lung disease, cardiovascular diseases, osteoarthritis, viral disease, cancer, and diabetes.

42.18. The method as claimed in any one of the claims 1-3, 7 or 10, ~~or 13, or 14,~~ wherein the nucleic acid is either cDNA or RNA.

43. ~~The method as claimed in claim 29, wherein the nucleic acid is selected from the group consisting of normal RNA, normal DNA, tumor RNA, or tumor DNA from the sample.~~

44.19. The method as claimed in any one of the claims 1-3, 7 or 10, ~~or 13, or 14,~~ wherein the enriching of the very small embryonic-like stem cells from the blood sample is by any method selected from the group consisting of flow cytometry, magnetic bead-based separation, filtration, microfluidic-based cell sorting, aptamer-based cell isolation, and buoyancy activated cell sorting.

20. The method as claimed in claim 2, wherein an increase of less than 3 folds in the expression level of Oct4A in the very small embryonic like stem cells from the blood sample as compared to the expression level of Oct4A in the control sample indicates an absence of cancer in the subject.

45. ~~The method as claimed in claim 14, wherein the method further comprises analysing the expression level of the cancer related marker in the nucleic acid obtained in step (c).~~

46. ~~The method as claimed in claim 32, wherein the expression level of the marker is analysed by using quantitative PCR techniques.~~

47. ~~The method as claimed in any one of the claims 1-3, 10, 13, or 14, wherein the method is able to detect cancer without the intratumor heterogeneity.~~

48. ~~The method as claimed in claim 14, wherein co-relating the sequence profile with a reference sequence profile to identify the presence or absence of a mutation in the marker is done by an algorithm.~~

49. ~~The method as claimed in claim 14, wherein comparing the expression level of the biomarker of very small embryonic-like stem cell in the sample with an expression~~

level of the at least one biomarker in a control sample and co-relating the sequence profile with a reference sequence profile to identify the presence or absence of a mutation in at least one marker are done by an algorithm.

50. The method as claimed in any one of the claims 1-3, 10, 13, or 14, wherein the nucleic acid represents a genome.

51. The method as claimed in any one of the claims 1-3, 10, 13, or 14, wherein the nucleic acid represents a transcriptome.

52. The method as claimed in any one of the claims 1-3, 10, 13, or 14, wherein the nucleic acid represents an exome.

53. The method as claimed in any one of the claims 1-3, 10, 13, or 14, wherein the nucleic acid represents cDNA.

54. The method as claimed in any one of the claims 1-3, 10, 13, or 14, wherein the method encompasses all the organs of a human subject in identifying a medical condition.

55. The method as claimed in any one of the claims 1-3, 10, 13, or 14, wherein the method provides information equivalent to all organ biopsy.

56. The method as claimed in any one of the claims 1-3, 10, 13, or 14, wherein the method is an *in vitro* method.

57. The method as claimed in any one of the claims 1-3, 10, 13, or 14, wherein the sample is selected from the group consisting of blood, tissue, urine, and sputum.

58. The method as claimed in claim 44, wherein the sample is blood, and wherein the sample is at least one cell type in the blood, and wherein the at least one cell type is selected from the group consisting of cancer stem cell, and circulating tumor cells.

59. A reagent kit comprising reagents for enriching very small embryonic-like stem cell from a blood sample.

60. 21. Use of Aa detection kit for detecting presence of a medical condition, the kit comprising: (a) primer set for analysing expression level of at least one biomarker selected from the group consisting of Oct4A, Stella, and Frigilis in a mixture

comprising very small embryonic-like stem cell; (b) reagents for performing quantitative PCR assay; (c) reagents for performing whole genome or exome or transcriptome sequencing; and (d) at least one tissue-specific array for analysing a sequence profile, wherein the medical condition is selected from the group consisting of diabetes, tuberculosis, Alzheimer's disease, dementia, cardiovascular disease, and arthritis.

~~61.22.~~ 22. A method for detecting presence of cancer in a subject, said method comprising: ~~(a) obtaining a blood/tissue sample from a subject;~~ (ba) enumerating the number of very small embryonic like stem cells in the blood sample of a subject; and ~~(eb)~~ (eb) comparing the number of very small embryonic like stem cells in the blood sample with the number of very small embryonic like stem cells in a control blood sample, wherein an increase in the number of very small embryonic like stem cells in the blood sample as compared to the number of very small embryonic like stem cells in a control blood sample detects the presence of cancer in the subject.

~~62.23.~~ 23. A method for predicting the onset of cancer in a subject, said method comprising: ~~(a) obtaining a blood/tissue sample from a subject;~~ (ba) enumerating the number of very small embryonic like stem cells in the blood sample of a subject; and ~~(eb)~~ (eb) comparing the number of very small embryonic like stem cells in the blood sample with the number of very small embryonic like stem cells in a control blood sample, wherein an increase in the number of very small embryonic like stem cells in the blood sample as compared to the number of very small embryonic like stem cells in a control blood sample predicts the onset of cancer in the subject.

~~63.24.~~ 24. A method for detecting the presence of a medical condition in a subject, said method comprising: ~~(a) obtaining a blood/tissue sample from a subject;~~ ~~(ba)~~ enriching very small embryonic like stem cells from the blood sample of a subject to obtain a mixture comprising said very small embryonic like stem cells; ~~(eb)~~ (eb) enumerating the number of very small embryonic like stem cells in the blood sample; and ~~(ec)~~ (ec) comparing the number of very small embryonic like stem cells in the blood

sample with the number of very small embryonic like stem cells in a control blood sample, wherein an increase in the number of very small embryonic like stem cells in the blood sample as compared to the number of very small embryonic like stem cells in a control blood sample detects the presence of a medical condition in the subject.

64. ~~A method for detecting presence of cancer in a subject, said method comprising: (a) obtaining a blood/tissue sample from a subject; (b) enriching very small embryonic like stem cells from the sample to obtain a mixture comprising said very small embryonic like stem cells; (c) enumerating *in vivo* the number of very small embryonic like stem cells in the blood/tissue of a subject; and d) comparing the number of very small embryonic like stem cells in the subject with the number of very small embryonic like stem cells in a control, wherein an increase in the number of very small embryonic like stem cells in the subject as compared to the number of very small embryonic like stem cells in a control detects the presence of cancer in the subject.~~

65. ~~A method for predicting the onset of cancer in a subject, said method comprising: (a) obtaining a blood/tissue sample from a subject; (b) enriching very small embryonic like stem cells from the sample to obtain a mixture comprising said very small embryonic like stem cells; (c) enumerating *in vivo* the number of very small embryonic like stem cells in the blood/tissue of a subject; and (d) comparing the number of very small embryonic like stem cells in the subject with the number of very small embryonic like stem cells in a control, wherein an increase in the number of very small embryonic like stem cells in the subject as compared to the number of very small embryonic like stem cells in a control predicts the onset of cancer in the subject.~~

66. ~~A method for detecting presence of a medical condition in a subject, said method comprising: (a) obtaining a blood/tissue sample; (b) enriching very small embryonic like stem cells from the sample to obtain a mixture comprising said very small~~

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~~embryonic like stem cells; (c) enumerating *in vivo* the number of very small embryonic like stem cells in the blood/tissue of a subject; and d) comparing the number of very small embryonic like stem cells in the subject with the number of very small embryonic like stem cells in a control, wherein an increase in the number of very small embryonic like stem cells in the subject as compared to the number of very small embryonic like stem cells in a control detects the presence of medical condition in the subject.~~