comprising at least two distinguishable sub-populations of cells in a total population of cells; (b) dividing the sample into at least two parts; (c) incubating at least one part obtained in step (b) in the absence of a test compound and at least one part obtained in step (b) in the presence of a test compound; (d) determining the number of cells that exhibit a distinguishable phenotype in one of the at least two sub-populations ~~that exhibit a distinguishable phenotype~~, relative to the number of cells that exhibit the same phenotype in the total population of cells ~~that exhibit the same phenotype~~ in (i) the at least one part incubated in the presence of the test compound and (ii) in the at least one part incubated in the absence of the test compound; and (e) determining selectivity of the test compound to induce the phenotype referred to in (d) in the one sub population referred to in step (d) over all other subpopulations by dividing (i) through (ii) wherein the test compound selectively induces the phenotype referred to in (d) if (i) divided through (ii) is greater than 1, preferably greater than 1.05, 1.1, 1.5, 2, 3 most preferably 5, and selectively inhibits or reduces the phenotype referred to in (d) if it is less than 1, preferably less than 0.95, 0.9, 0.7, 0.5, 0.3, most preferably less than 0.2.

In another aspect, the present disclosure refers to a method for determining whether a subject suffering from cancer will respond or is responsive to treatment with a test compound, the method comprising the steps: (a) providing a sample obtained from the subject comprising at least two sub-populations of cells in a total population cells, wherein at least one sub-population corresponds to cancerous cells and at least one sub-population corresponds to non-cancerous cells; (b) dividing the sample into at least two parts; (c) incubating at least one part obtained in step (b) in the absence of a test compound and at least one part in the presence of a test compound; (d) determining the number of viable cells in at least one of the sub-population corresponding to cancer cells relative to the number of viable cells in the total population of cells in (i) the at least one part incubated in the presence of the test compound and (ii) the at least one part incubated in the absence of the test compound; and (e) determining whether the subject will respond or is responsive to treatment with the test compound by dividing (i) through (ii), wherein the subject will respond or is responsive to treatment if the resulting value is less than 1, preferably less than 0.95, 0.9, 0.8, 0.6, 0.4 most preferably less than 0.2.

Description

The invention, in a first embodiment, thus relates to a method for determining the selectivity of a test compound, the method comprising the steps:

Claims

1. A method for determining the selectivity of a test compound, the method comprising the steps:
   (a) providing a sample comprising at least two distinguishable sub-populations of cells in a total population of cells;
   (b) dividing the sample into at least two parts;
   (c) incubating at least one part obtained in step (b) in the absence of a test compound and at least one part obtained in step (b) in the presence of a test compound;
   (d) determining the number of cells that exhibit a distinguishable phenotype in one of the at least two sub-populations ~~that exhibit a distinguishable phenotype~~, relative to the number of cells that exhibit the same phenotype in the total population of cells ~~that exhibit the same phenotype~~ in
      (i) the at least one part incubated in the presence of the test compound and
      (ii) in the at least one part incubated in the absence of the test compound; and
   (e) determining selectivity of the test compound to induce the phenotype referred to in (d) in the one sub population referred to in step (d) over all other subpopulations by dividing (i) through (ii) wherein the test compound selectively induces the phenotype referred to in (d) if (i) divided through (ii) is greater than 1, preferably greater than 1.05, 1.1, 1.5, 2, 3 most preferably 5, and selectively inhibits or reduces the phenotype referred to in (d) if it is less than 1, preferably less than 0.95, 0.9, 0.7, 0.5, 0.3, most preferably less than 0.2.

2. The method according to claim 1, wherein the distinguishable phenotype in step (d) is viability and wherein
   (i) if the selectivity determined in step (e) is <1 the test compound is determined to selectively reduce the number of viable cells of the one sub-population of step (d), and
   (ii) if the selectivity determined in step (e) is >1 the test compound is determined to selectively improve viability of the one sub-population

and/or to selectively reduce the viability of one or more of the sub-population(s) other than the one sub-population of step (d).

3. A method for determining whether a subject suffering from cancer will respond or is responsive to treatment with a test compound, the method comprising the steps:
   (a) providing a sample obtained from the subject comprising at least two sub-populations of cells in a total population cells, wherein at least one sub-population corresponds to cancerous cells and at least one sub-population corresponds to non-cancerous cells;
   (b) dividing the sample into at least two parts;
   (c) incubating at least one part obtained in step (b) in the absence of a test compound and at least one part in the presence of a test compound;
   (d) determining the number of viable cells in at least one of the sub-populations corresponding to cancer cells relative to the number of viable cells in the total population of cells in
      (i) the at least one part incubated in the presence of the test compound and
      (ii) the at least one part incubated in the absence of the test compound; and
   (e) determining whether the subject will respond or is responsive to treatment with the test compound by dividing (i) through (ii), wherein the subject will respond or is responsive to treatment if the resulting value is less than 1, preferably less than 0.95, 0.9, 0.8, 0.6, 0.4 most preferably less than 0.2.

4. The method of claim 3, wherein the method is repeated for at least two test compounds and whether the subject will respond or is responsive to treatment with a combination of the at least two test compounds is determined by subtracting the values obtained in (e) for each of the at least two test compounds from 1.0, and summing over the resulting values for the at least two test compounds wherein if the resulting sum is greater than -1, preferably greater than -0.5, 0, 0.5, most preferably greater than 1, the subject is determined to respond or be responsive to treatment with the combination of the at least two test compounds.

5. The method according to any one of claims 1 to 4, wherein the test compound(s) comprise(s) one or more chemical substances.

6. The method according to any one of claims 1 to 5, wherein at least one part obtained in step (b) is further divided into at least two parts, wherein each of the at least two parts is incubated in step (c) with the test compound at different concentrations and wherein steps (d) and (e) are repeated for each concentration of the test compound independently to determine a selectivity/value at each concentration of the test compound whereby an average selectivity/value over all concentrations is calculated after step (e) and used for determining the final selectivity/value.

7. The method according to any one of claims 1 to 5, wherein in step (b) the sample is divided into at least three parts and in step (c) at least two parts are incubated in the absence of a test compound or at least two parts are incubated in the presence of a test compound whereby each part incubated in the presence of the test compound is incubated in the presence of the same concentration of the test compound, and wherein in step (d) the number of cells in the one of the at least two sub-populations that exhibit a distinguishable phenotype relative to the number of cells in the total population of cells that exhibit the same distinguishable phenotype is determined for

(i) each part incubated in the presence of the test compound independently and/or

(ii) each part incubated in the absence of the test compound independently and

the average of the relative numbers obtained in (i) and/or the average of the relative numbers obtained in (ii) is used.

8. The method according to any one of claims 1 to 5, wherein in step (b) the sample is divided into at least three parts and in step (c) at least one part is incubated in the absence of a test compound and/or at least two parts are incubated in the presence of at least two different concentrations of the test compound and in step (d) the number of cells in the one of the at least two sub-populations that exhibit a distinguishable phenotype relative to the number of cells in the total population of cells that exhibit the same distinguishable phenotype is determined for

(i) each part incubated in the presence of the test compound independently and/or

(ii) each part incubated in the absence of the test compound independently

wherein the average of (i) is determined for each concentration independently and/or the average of (ii) is determined and used for further steps and wherein in step (e) the selectivity/value is determined for each concentration of the test

compound by dividing the average of (i) for each concentration through the average of (ii) and the final selectivity/value is obtained by averaging the selectivity/value for each concentration.

9. The method according to any one of claims 3 or 5-8, wherein the method is repeated for at least two test compounds and the test compound with the lowest value obtained in step (e) is selected for treatment of the subject suffering from cancer.

10. The method according to any one of claims 4 to 8, wherein the method is repeated for at least three test compounds and the combination of at least two of the at least three test compounds with the highest value obtained by subtracting the values obtained in (e) for each of the at least two test compounds in the combination from 1.0, and summing over the resulting values for the at least two test compounds in the combination, is selected for treatment of the subject suffering from cancer.

11. The method according to claims 3, 4, 9 or 10, wherein the cancer is a cancer associated with PBMCs or bone marrow cells or cells derived from PBMCs or bone marrow cells.

12. The method according to any one of claims 1 to 11, wherein the sample is a tissue sample that contains at least 1% cancerous cells and/or at least 1% non-cancerous cells.

13. The method according to claim 12, wherein the tissue sample is cultured as a non-adherent cell monolayer.

14. The method according to claim 13, wherein the number of viable cancerous and non-cancerous cells is determined using automated microscopy.

15. The method according to claim 14, wherein the number of viable cells is determined as the number of non-fragmented nuclei.