Furthermore, in the second to fifth embodiment, multiplication coefficients associated to a mutation Z_1, z_2 and Z_3 are 1 when no mutation exists and, depending on the functional impact of the mutation, can be comprised between 10 and 1,000.

One aspect of the invention relates to a method for predicting the relative efficacy of a plurality of drugs for treating a cancer in a patient comprising: - characterizing molecular anomalies of a tumour sample from the patient in comparison to a normal sample from the same patient, thereby determining the deregulated genes in the tumour; - providing a database comprising the target genes for each drug of the plurality of drugs; - determining a score for each drug of the plurality of drugs essentially based on the percentage of deregulated genes among the target genes for each drug in the tumour sample from the patient, thereby a higher score is predictive of a higher relative efficacy of the drug for treating the tumour in the patient.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 : Thoracic scanner in October 2005 of the patient of Example 1.

Figure 2 : Thoracic scanner in November 2008 of the patient of Example 1.

Figure 3 : Thoracic scanner in April 2009 of the patient of Example 1.

Figure 4 : Thoracic scanner in July 2009 of the patient of Example 1.

Figure 5 : Thoracic scanners in January and March 2010 of the patient of Example 3.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides a new concept for selecting the most appropriate therapy at the individual level. The drug selection is based on the biologic characteristics of the tumor of the individual to be treated in comparison to a normal sample from the same individual. Based on a score essentially based on the percentage of deregulated target genes or microRNAs for each drug, the relative efficacy of the drugs can be predicted for the individual in order to treat the specific tumour.

General Concept

It is at the level of the optimal therapeutic strategy choice that applies the object of the present invention. For selecting the most appropriate therapeutic strategy, the method of the present invention is taking into account of, on one hand, the biological data of the tumor to be treated as a whole and, on the other hand, a plurality of drugs, preferably all existing drugs (either registered or in development). A score is determined for each drug based on the biological characteristics of the specific tumour to be treated for a given subject. This score makes it

possible to order the various drugs in decreasing order for their potential efficacy. The physician can use these scores to select the optimal drug or combination of drugs for the given subject. This approach, allowing the association of each drug with a score depending on the biological characteristics of the tumour, constitutes the basis of this invention. Therefore, this invention is likely to meet the present needs for personalized medicine.

The method can be used both for registered drugs and for developed drugs (e.g., temporary authorization of use or clinical trials).

WHAT IS CLAIMED

1- A method for predicting the relative efficacy of a plurality of drugs for treating a cancer in a patient comprising:

- characterizing molecular anomalies of a tumour sample from the patient in comparison to a normal sample from the same patient, thereby determining the deregulated genes in the tumour;

- providing a database comprising the target genes for each drug of the plurality of drugs;

- determining a score for each drug of the plurality of drugs essentially based on the percentage of deregulated genes among the target genes for each drug in the tumour sample from the patient, thereby a higher score is predictive of a higher relative efficacy of the drug for treating the tumour in the patient.

2- The method according to claim 1, wherein the step of characterizing molecular anomalies of a tumour sample comprises determining the genes differentially expressed in the tumour in comparison to the normal sample, and/or determining the gain or loss of gene copy number and/or detecting the presence of a mutation in a gene.

3- The method according to claim 2, wherein the step of characterizing molecular anomalies of a tumour sample comprises determining a fold change (F) for the differentially expressed genes and/or for the gain or loss of gene copy number and, optionally, further determining the intensity of the gene transcription (Int) for the differentially expressed genes.

4- The method according to anyone of claims 1-3, wherein the target genes for each drug are classified in the database into the major target genes (MC), the minor target genes (Mc) and the resistance genes (CR).

5- The method according to anyone of claims 1-4, wherein the score (W) for a given drug is determined by the following algorithm:

$$W = P\,z\,\frac{(\Sigma_C F_{c>2})}{n_c F_{c>2}}$$

wherein

W is the score for the given drug ;

P is the percentage of target genes for the given drug which are deregulated in the tumour of the patient;

z is an optional multiplication coefficient associated to the presence of a mutation in a target gene of the given drug ;

Σ is sum ;

Fc>2 is the fold change of each deregulated target gene for the given drug with a Fold Change higher than 2;

$nC_{Fc>2}$ refers to the number of target genes for the given drug with a Fold Change higher than 2.

6- The method according to claim 5, wherein Fc>2 is the Fold Change of each over-expressed target gene for the given drug with a Fold Change higher than 2 and $nC_{Fc>2}$ is either the number of target genes for the given drug with a Fold Change higher than 2, or the number of over-expressed target genes for the given drug with a Fold Change higher than 2.

7- The method according to anyone of claims 1-4, wherein the score (W) for a given drug is determined by the following algorithm:

$$W = P\left[\frac{(\Sigma_{CM} F_{CM})}{n_1 CM} q_1 z_1 + \frac{(\Sigma_{Cm} F_{Cm})}{n_2 Cm} q_2 z_2 - \frac{(\Sigma_{CR} F_{CR})}{n_3 CR} q_3 z_3\right]$$

wherein

W is the score for the given drug;

P is the percentage of target genes for the given drug which are deregulated in the tumour of the patient;

Σ is sum ;

CM refers to major target genes for the given drug;

Cm refers to minor target genes for the given drug;

CR refers to resistance genes for the given drug;

n_1CM, n_2Cm and n_3CR are respectively the number of deregulated target genes with a defined threshold for major target genes, minor target genes and resistance genes;

F_{CM}, F_{Cm} and F_{CR} are the Fold change of each gene higher than the defined threshold for major target genes, minor target genes and resistance genes, respectively;

q_1, q_2 and q_3 are optional multiplication coefficients for major target genes, minor target genes and resistance genes, respectively;

z_1, z_2 and z_3 are optional multiplication coefficients associated to the presence of a mutation in a major target gene, a minor target gene and a resistance gene, respectively.

8- The method according to anyone of claims 1-4, wherein the score (W) for a given drug is determined by the following algorithm:

$$W = \frac{P_{CM}(\Sigma_{CM} F_{CM})}{n_1 CM} q_1 z_1 + \frac{P_{Cm}(\Sigma_{Cm} F_{Cm})}{n_2 Cm} q_2 z_2 - \frac{P_{CR}(\Sigma_{CR} F_{CR})}{n_3 CR} q_3 z_3$$

wherein the meaning of W, Σ, CM, Cm, CR, F_{CM}, F_{Cm}, F_{CR}, q_1, q_2, q_3, z_1, z_2 and z_3 are as defined above and P_{CM}, P_{Cm} and P_{CR} are the percentage of genes for the given drug which are deregulated in the tumour of the individual for major target genes, minor target genes and resistance genes, respectively

9- The method according to anyone of claims 1-4, wherein the score (W) for a given drug is determined by one of the following algorithms:

$$W = P\left[\frac{(\Sigma_{CM} F_{CM} \times Int_{CM})}{n_1 CM} q_1 z_1 + \frac{(\Sigma_{Cm} F_{Cm} \times Int_{Cm})}{n_2 Cm} q_2 z_2 - \frac{(\Sigma_{CR} F_{CR} \times Int_{CR})}{n_3 CR} q_3 z_3\right]$$

or

$$W = \frac{P_{CM}(\Sigma_{CM} F_{CM} \times Int_{CM})}{n_1 CM} q_1 z_1 + \frac{P_{Cm}(\Sigma_{Cm} F_{Cm} \times Int_{Cm})}{n_2 Cm} q_2 z_2 - \frac{P_{CR}(\Sigma_{CR} F_{CR} \times Int_{CR})}{n_3 CR} q_3 z_3$$

wherein the meaning of W, Σ, CM, Cm, CR, F_{CM}, F_{Cm}, F_{CR}, q_1, q_2, q_3, z_1, z_2 and z_3, and if present P_{CM}, P_{Cm} and P_{CR}, are as defined above and Int_{CM}, Int_{Cm} and Int_{CR} are the intensity for major target genes, minor target genes and resistance genes, respectively.

10- The method according to anyone of claims 1-4, wherein the score (W) for a given drug is determined by one of the following algorithms:

$$W = P\left[\frac{(\Sigma_{CM} F_{CM})}{n_1 CM} q_1 z_1 - \frac{(\Sigma_{CR} F_{CR})}{n_3 CR} q_3 z_3\right]$$

$$W = \frac{P_{CM}(\Sigma_{CM} F_{CM})}{n_1 CM} q_1 z_1 - \frac{P_{CR}(\Sigma_{CR} F_{CR})}{n_3 CR} q_3 z_3$$

or

$$W = P\left[\frac{(\Sigma_{CM} F_{CM} \times Int_{CM})}{n_1 CM} q_1 z_1 - \frac{(\Sigma_{CR} F_{CR} \times Int_{CR})}{n_3 CR} q_3 z_3\right]$$

or

$$W = \frac{P_{CM}(\Sigma_{CM} F_{CM} \times Int_{CM})}{n_1 CM} q_1 z_1 - \frac{P_{CR}(\Sigma_{CR} F_{CR} \times Int_{CR})}{n_3 CR} q_3 z_3$$

wherein the meaning of W, Σ, CM, CR, F_{CM}, F_{CR}, q_1, q_3, z_I and z_3, and if present P_{CM}, P_{CR}, Int_{CM}, and Int_{CR} are as defined above.

11- The method according to anyone of claims 7-10, wherein F_{CM}, F_{Cm} and F_{CR} are the Fold Change of each over-expressed target gene for the given drug with the defined threshold and n_1CM, n_2Cm and n_3CR are either the number of target genes for the given drug with the defined threshold, or the number of over-expressed target genes for the given drug with the defined threshold.

12- The method according to claim 11, wherein the defined threshold is a Fold change of at least 2 or higher than 2.

13- The method according to anyone of claims 7-12, wherein multiplication coefficients for the target genes can be comprised between 10 and 1,000 for major target genes (q_1), 0.1 and 10 for minor target genes (q_2) and 10 to 1,000 for resistance genes (q_3).

14- The method according to anyone of claims 7-13, wherein multiplication coefficients associated to a mutation z_1, z_2 and z_3 are 1 when no mutation exists and, depending on the functional impact of the mutation, can be comprised between 10 and 1,000.

CLAIMS

1. A method for predicting the relative efficacy of a plurality of drugs for treating a cancer in a patient comprising:

- characterizing molecular anomalies of a tumour sample from the patient in comparison to a normal sample from the same patient, thereby determining the deregulated genes in the tumour;
- providing a database comprising the target genes for each drug of the plurality of drugs;
- determining a score for each drug of the plurality of drugs essentially based on the percentage of deregulated genes among the target genes for each drug in the tumour sample from the patient, thereby a higher score is predictive of a higher relative efficacy of the drug for treating the tumour in the patient.

2. The method according to claim 1, wherein the step of characterizing molecular anomalies of a tumour sample comprises determining the genes differentially expressed in the tumour in comparison to the normal sample, and/or determining the gain or loss of gene copy number and/or detecting the presence of a mutation in a gene.

3. The method according to claim 2, wherein the step of characterizing molecular anomalies of a tumour sample comprises determining a fold change (F) for the differentially expressed genes and/or for the gain or loss of gene copy number and, optionally, further determining the intensity of the gene transcription (Int) for the differentially expressed genes.

4. The method according to any one of claims 1-3, wherein the target genes for each drug are classified in the database into the major target genes (MC), the minor target genes (Mc) and the resistance genes (CR).

5- The method according to anyone of claims 1-4, wherein the score (W) for a given drug is determined by the following algorithm:

$$W = P\,z\,\frac{(\Sigma_C F_{c>2})}{n_C F_{c>2}}$$

wherein

W is the score for the given drug;

P is the percentage of target genes for the given drug which are deregulated in the tumour of the patient;

z is an optional multiplication coefficient associated to the presence of a mutation in a target gene of the given drug ;

Σ is sum;

$F_{c>2}$ is the fold change of each deregulated target gene for the given drug with a Fold Change higher than 2;

$n_C F_{c>2}$ refers to the number of target genes for the given drug with a Fold Change higher than 2.

6. The method according to claim 5, wherein $F_{c>2}$ is the Fold Change of each over-expressed target gene for the given drug with a Fold Change higher than 2 and $n_C F_{C>2}$ is either the number of target genes for the given drug with a Fold Change higher than 2, or the number of over-expressed target genes for the given drug with a Fold Change higher than 2.

7. The method according to any one of claims 1-4, wherein the score (W) for a given drug is determined by the following algorithm:

$$W = P\left[\frac{(\Sigma_{CM} F_{CM})}{n_1 CM} q_1 z_1 + \frac{(\Sigma_{Cm} F_{Cm})}{n_2 Cm} q_2 z_2 - \frac{(\Sigma_{CR} F_{CR})}{n_3 CR} q_3 z_3\right]$$

wherein

W is the score for the given drug;

P is the percentage of target genes for the given drug which are deregulated in the tumour of the patient;

Σ is sum;

CM refers to major target genes for the given drug;

Cm refers to minor target genes for the given drug;

CR refers to resistance genes for the given drug;

n_1CM, n_2Cm and n_3CR are respectively the number of deregulated target genes with a defined threshold for major target genes, minor target genes and resistance genes;

FCM, Fcm and FCR are the Fold change of each gene higher than the defined threshold for major target genes, minor target genes and resistance genes, respectively;

q_1, q_2 and q_3 are optional multiplication coefficients for major target genes, minor target genes and resistance genes, respectively;

z_1, z_2 and z_3 are optional multiplication coefficients associated to the presence of a mutation in a major target gene, a minor target gene and a resistance gene, respectively.

8. The method according to any one of claims 1-4, wherein the score (W) for a given drug is determined by the following algorithm:

$$W = \frac{P_{CM}(\Sigma_{CM} F_{CM})}{n_1 CM} q_1 z_1 + \frac{P_{Cm}(\Sigma_{Cm} F_{Cm})}{n_2 Cm} q_2 z_2 - \frac{P_{CR}(\Sigma_{CR} F_{CR})}{n_3 CR} q_3 z_3$$

wherein the meaning of W, Σ, CM, Cm, CR, F_{CM}, Fcm, F_{CR}, q_1, q_2, q_3, z_1, z_2 and z_3 are as defined above and P_{CM}, P_{cm} and P_{CR} are the percentage of genes for the given drug which are deregulated in the tumour of the individual for major target genes, minor target genes and resistance genes, respectively.

9. The method according to any one of claims 1-4, wherein the score (W) for a given drug is determined by one of the following algorithms:

$$W = P\left[\frac{(\Sigma_{CM} F_{CM} \times Int_{CM})}{n_1 CM} q_1 z_1 + \frac{(\Sigma_{Cm} F_{Cm} \times Int_{Cm})}{n_2 Cm} q_2 z_2 - \frac{(\Sigma_{CR} F_{CR} \times Int_{CR})}{n_3 CR} q_3 z_3\right]$$

or

$$W = \frac{P_{CM}(\Sigma_{CM} F_{CM} \times Int_{CM})}{n_1 CM} q_1 z_1 + \frac{P_{Cm}(\Sigma_{Cm} F_{Cm} \times Int_{Cm})}{n_2 Cm} q_2 z_2 - \frac{P_{CR}(\Sigma_{CR} F_{CR} \times Int_{CR})}{n_3 CR} q_3 z_3$$

wherein the meaning of W, Σ, CM, Cm, CR, F_{CM}, F_{cm}, F_{CR}, q_1, q_2, q_3, z_1, z_2 and z_3, and if present P_{CM}, P_{cm} and P_{CR}, are as defined above and Int_{CM}, Int_{cm} and Int_{CR} are the intensity for major target genes, minor target genes and resistance genes, respectively.

10. The method according to any one of claims 1-4, wherein the score (W) for a given drug is determined by one of the following algorithms:

$$W = P\left[\frac{(\Sigma_{CM} F_{CM})}{n_1 CM} q_1 z_1 - \frac{(\Sigma_{CR} F_{CR})}{n_3 CR} q_3 z_3\right]$$

$$W = \frac{P_{CM}(\Sigma_{CM} F_{CM})}{n_1 CM} q_1 z_1 - \frac{P_{CR}(\Sigma_{CR} F_{CR})}{n_3 CR} q_3 z_3$$

or

$$W = P\left[\frac{(\Sigma_{CM} F_{CM} \times Int_{CM})}{n_1 CM} q_1 z_1 - \frac{(\Sigma_{CR} F_{CR} \times Int_{CR})}{n_3 CR} q_3 z_3\right]$$

or

$$W = \frac{P_{CM}(\Sigma_{CM} F_{CM} \times Int_{CM})}{n_1 CM} q_1 z_1 - \frac{P_{CR}(\Sigma_{CR} F_{CR} \times Int_{CR})}{n_3 CR} q_3 z_3$$

wherein the meaning of W, Σ, CM, CR, F_{CM}, F_{CR}, q_1, q_3, z_1 and z_3, and if present P_{CM}, P_{CR}, Int_{CM}, and Int_{CR} are as defined above.

11. The method according to any one of claims 7-10, wherein F_{CM}, F_{cm} and F_{CR} are the Fold Change of each over-expressed target gene for the given drug with the defined threshold and n_1CM, n_2Cm and n_3CR are either the number of target genes for the given drug with the defined threshold, or the number of over-expressed target genes for the given drug with the defined threshold.

12. The method according to claim 11, wherein the defined threshold is a Fold change of at least 2 or higher than 2.

13. The method according to any one of claims 7-12, wherein multiplication coefficients for the target genes can be comprised between 10 and 1,000 for major

target genes (q_1), 0.1 and 10 for minor target genes (q_2) and 10 to 1,000 for resistance genes (q_3).

14. The method according to any one of claims 7-13, wherein multiplication coefficients associated to a mutation z_1, z_2 and z_3 are 1 when no mutation exists and, depending on the functional impact of the mutation, can be comprised between 10 and 1,000.