

METHOD OF PREDICTING CLINICAL OUTCOME OF ANTICANCER AGENTS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority from U.S. Provisional Patent Application No. 62/456,550, filed February 8, 2017; U.S. Provisional Patent Application No. 62/464,993, filed February 28, 2017; and U.S. Provisional Patent Application No. 62/596,060, filed December 7, 2017, the contents of each of which are incorporated herein by reference in its entirety.

TECHNICAL FIELD

[0002] This application pertains to prognostic and therapeutic methods involving determining the responsiveness of an individual having cancer to one or more therapeutic agents based on a clinical response predictor.

BACKGROUND

[0003] Cultured tumor tissue explants derived from patients have been used to predict responsiveness to administration of anticancer therapies in efforts to select appropriate drug treatment regimens for a given patient. However, predictions based on such tumor tissue cultures are prone to yielding false positives and false negatives. The selection of both the tumor tissue culture conditions and the combination of assays carried out on the tumor tissue cultures plays an important role in the accuracy and sensitivity of methods of predicting responsiveness to anticancer therapies based on these cultures. There is an unmet need to improve and refine methods of assessing responsiveness to anticancer therapies using patient-derived tumor tissue cultures.

SUMMARY

[0003a] In one aspect, the present disclosure refers to a method of predicting responsiveness of an individual having a cancer to administration of an anticancer drug regimen, the method comprising: a) obtaining a readout comprising an assessment score for each of a plurality of assays conducted on a tumor tissue culture treated with the anticancer drug regimen, wherein the tumor tissue culture comprises a tumor tissue from the individual cultured on a tumor microenvironment platform, and wherein the plurality of assays comprises a first set of a plurality of assays and a second set of one or more assays, wherein the second set of one or more assays comprises determining i) an amount of an immune cell in a region of tumor cells in the tumor tissue culture and ii) an amount of the immune cell in a

region of normal stroma in the tumor tissue culture; b) inputting the readout into a predictive model; c) using the predictive model to generate an output; and d) using the output to predict responsiveness of the individual to administration of the anticancer drug regimen. In another aspect, the present disclosure refers to a method of classifying likely responsiveness of an individual having a cancer to administration of an anticancer drug regimen, comprising: a) obtaining a readout comprising an assessment score for each of a plurality of assays conducted on a tumor tissue culture treated with the anticancer drug regimen, wherein the tumor tissue culture comprises a tumor tissue from the individual cultured on a tumor microenvironment platform, and wherein the plurality of assays comprises a first set of a plurality of assays and a second set of one or more assays, wherein the second set of one or more assays comprises determining i) an amount of an immune cell in a region of tumor cells in the tumor tissue culture and ii) an amount of the immune cell in a region of normal stroma in the tumor tissue culture; b) inputting the readout into a predictive model; c) using the predictive model to generate an output; and d) using the output to classify the likely responsiveness of the individual to administration of the anticancer drug regimen. In another aspect, the present disclosure refers to a computer-implemented method for predicting responsiveness of an individual having a cancer to administration of an anticancer drug regimen, the method comprising: a) accessing a readout comprising an assessment score for each of a plurality of assays conducted on a tumor tissue culture treated with the anticancer drug regimen, wherein the tumor tissue culture comprises a tumor tissue from the individual cultured on a tumor microenvironment platform, and wherein the plurality of assays comprises a first set of a plurality of assays and a second set of one or more assays, wherein the second set of one or more assays comprises determining i) an amount of an immune cell in a region of tumor cells in the tumor tissue culture and ii) an amount of the immune cell in a region of normal stroma in the tumor tissue culture; b) inputting the readout into a predictive model; c) using the predictive model to generate an output; and d) using the output to predict responsiveness of the individual to administration of the anticancer drug regimen. In yet another aspect, the present disclosure refers to the use of an anticancer drug regimen to which the individual is predicted to respond according to the method of the present disclosure in the manufacture of a medicament for treating cancer in an individual in need thereof. In yet another aspect, the present disclosure refers to a method comprising : a) culturing a tumor tissue obtained from an individual on a tumor microenvironment platform to obtain a tumor tissue culture, b) conducting an assay on the tumor tissue culture treated with an anticancer

drug regimen; wherein the assay comprises determining i) an amount of an immune cell in a region of tumor cells in the tumor tissue culture and ii) an amount of the immune cell in a region of normal stroma in the tumor tissue culture.

[0004] In some examples, there is provided a method of predicting responsiveness of an individual having a cancer to administration of an anticancer drug regimen, the method comprising: a) obtaining a readout comprising an assessment score for each of a plurality of assays conducted on a tumor tissue culture treated with the anticancer drug regimen, wherein the tumor tissue culture comprises a tumor tissue from the individual cultured on a tumor microenvironment platform, wherein the plurality of assays comprises a first set of a plurality of assays and a second set of one or more assays, and wherein the second set of one or more assays comprises an assay for tumor infiltration of an immune cell; b) inputting the readout into a predictive model; c) using the predictive model to generate an output; and d) using the

output to predict responsiveness of the individual to administration of the anticancer drug regimen.

[0005] In some examples, there is provided a method of classifying likely responsiveness of an individual having a cancer to administration of an anticancer drug regimen, comprising: a) obtaining a readout comprising an assessment score for each of a plurality of assays conducted on a tumor tissue culture treated with the anticancer drug regimen, wherein the tumor tissue culture comprises a tumor tissue from the individual cultured on a tumor microenvironment platform, wherein the plurality of assays comprises a first set of a plurality of assays and a second set of one or more assays, and wherein the second set of one or more assays comprises an assay for tumor infiltration of an immune cell; b) inputting the readout into a predictive model; c) using the predictive model to generate an output; and d) using the output to classify the likely responsiveness of the individual to administration of the anticancer drug regimen.

[0006] In some examples, there is provided a computer-implemented method for predicting responsiveness of an individual having a cancer to administration of an anticancer drug regimen, the method comprising: a) accessing a readout comprising an assessment score for each of a plurality of assays conducted on a tumor tissue culture treated with the anticancer drug regimen, wherein the tumor tissue culture comprises a tumor tissue from the individual cultured on a tumor microenvironment platform, wherein the plurality of assays comprises a first set of a plurality of assays and a second set of one or more assays, and wherein the second set of one or more assays comprises an assay for tumor infiltration of an immune cell; b) inputting the readout into a predictive model; c) using the predictive model to generate an output; and d) using the output to predict responsiveness of the individual to administration of the anticancer drug regimen.

[0007] In some examples, according to any of the methods described above, the predictive model comprises an algorithm that uses each of the assessment scores as input and generates the output. In some examples, the algorithm comprises multiplying each of the input assessment scores with a corresponding weightage coefficient to obtain a plurality of weighted assessment scores; and combining the plurality of weighted assessment scores to generate the output.

[0008] In some examples, according to any of the methods described above, the predictive model comprises a first algorithm that uses each of the assessment scores for the first set of a plurality of assays as input and generates a preliminary output, and a second

algorithm that uses the preliminary output and each of the assessment scores for the second set of one or more assays as input and generates the output. In some examples, the first algorithm comprises multiplying each of the input assessment scores with a corresponding weightage coefficient to obtain a plurality of weighted assessment scores; and combining the plurality of weighted assessment scores to generate the preliminary output. In some examples, the preliminary output predicts a primary degree of responsiveness of the individual to administration of the anticancer drug regimen, and wherein the second algorithm comprises adjusting the primary predicted degree of responsiveness based on the input assessment scores to generate the output. In some examples, the second set of one or more assays consists of the assay for tumor infiltration of an immune cell, and adjusting the primary predicted degree of responsiveness comprises predicting a secondary degree of responsiveness of the individual to administration of the anticancer drug regimen based on the input assessment score, and 1) adjusting the primary predicted degree of responsiveness by decreasing the predicted degree of responsiveness if the secondary predicted degree of responsiveness is lower than the primary predicted degree of responsiveness and the input assessment score is below a first threshold, thereby generating the output ; or 2) adjusting the primary predicted degree of responsiveness by increasing the predicted degree of responsiveness if the secondary predicted degree of responsiveness is greater than the primary predicted degree of responsiveness and the input assessment score is above a second threshold, thereby generating the output.

[0009] In some examples, according to any of the methods described above, the output predicts complete clinical response, partial clinical response, or no clinical response of the individual to administration of the anticancer drug regimen.

[0010] In some examples, according to any of the methods described above, the output predicts response or no response of the individual to administration of the anticancer drug regimen.

[0011] In some examples, according to any of the methods described above, the assay for tumor infiltration of an immune cell comprises determining the amount of the immune cell in a region of tumor cells in the tumor tissue culture. In some examples, the assay for tumor infiltration of an immune cell comprises determining the ratio of i) the amount of the immune cell in a region of tumor cells in the tumor tissue culture to ii) the amount of the immune cell in a region of normal stroma in the tumor tissue culture.

[0012] In some examples, according to any of the methods described above, the immune cell is an NK cell.

[0013] In some examples, according to any of the methods described above, the first set of a plurality of assays is selected from the group consisting of cell viability assays, cell death assays, cell proliferation assays, tumor morphology assays, tumor stroma content assays, cell metabolism assays, senescence assays, cytokine profile assays, enzyme activity assays, tumor and/or stromal cell expression assays, and any combination thereof.

[0014] In some examples, according to any of the methods described above, the tumor microenvironment platform comprises an extracellular matrix composition comprising one or more of collagen 1, collagen 3, collagen 4, collagen 6, Fibronectin, Vitronectin, Cadherin, Filamin A, Vimentin, Osteopontin, Laminin, Decorin, and Tenascin C. In some examples, the tumor microenvironment platform further comprises serum, plasma, and/or peripheral blood nuclear cells (PBNCs). In some examples, one or more of the serum, plasma, and/or PBNCs are derived from the individual.

[0015] In some examples, according to any of the methods described above, step a) further comprises conducting the plurality of assays on the tumor tissue culture and/or step a) further comprises preparing the tumor tissue culture by culturing tumor tissue from the individual on the tumor microenvironment platform.

[0016] In some examples, according to any of the methods described above, the assessment scores are generated based on a comparison between i) the results of the plurality of assays conducted on the tumor tissue culture treated with the anticancer drug regimen; and ii) the results of the plurality of assays conducted on a reference tumor tissue culture, wherein the reference tumor tissue culture comprises a tumor tissue from the individual cultured on the tumor microenvironment platform. In some examples, the reference tumor tissue culture is not treated with the anticancer drug regimen. In some examples, step a) further comprises conducting the plurality of assays on the reference tumor tissue culture; and/or step a) further comprises preparing the reference tumor tissue culture by culturing tumor tissue from the individual on the tumor microenvironment platform.

[0017] In some examples, there is provided a method of treating cancer in an individual in need thereof, the method comprising administering to the individual an anticancer drug regimen to which the individual is predicted to respond according to any of the methods described above. In some examples, the individual is predicted to have a

complete clinical response or partial clinical response to administration of the anticancer drug regimen.

[0018] In some examples, according to any of the methods described above, the anticancer drug regimen comprises an anticancer agent and/or an immunotherapeutic agent. In some examples, the anticancer drug regimen comprises an anticancer agent. In some examples, the anticancer drug regimen comprises an immunotherapeutic agent. In some examples, the anticancer drug regimen comprises an anticancer agent and an immunotherapeutic agent. In some examples, the anticancer agent is selected from the group consisting of adriamycin, gemcitabine, palbociclib, docetaxel, fulvestrant, carboplatin, exemestane, everolimus, vinorelbine, olaparib, capecitabine, cyclophosphamide, methotrexate, fluorouracil, and any combination thereof. In some examples, the immunotherapeutic agent is an immune checkpoint inhibitor. In some examples, the immunotherapeutic agent is selected from the group consisting of nivolumab, ipilimumab, pembrolizumab, atezolizumab, and any combination thereof.

[0019] In some examples, there is provided a method of predicting responsiveness to a therapeutic agent for treating cancer in an individual in need thereof, the method comprising: a) obtaining a readout comprising assessment scores from a plurality of assays conducted on a tumor tissue culture, wherein the tumor tissue culture comprises i) a tumor microenvironment platform cultured with tumor tissue from the individual; and ii) the therapeutic agent; b) converting the readout into a sensitivity index; and c) using the sensitivity index to predict responsiveness to the therapeutic agent, wherein at least one of the plurality of assays does not relate to a tumor cell phenotype.

[0020] In some examples, according to any of the methods described above, the plurality of assays is selected from the group consisting of cell viability assays, cell death assays, cell proliferation assays, tumor morphology assays, tumor stroma content assays, cell metabolism assays, senescence assays, cytokine profile assays, enzyme activity assays, tumor and/or stromal cell expression assays, immune cell contexture assays, and any combination thereof. In some examples, at least one of the plurality of assays comprises quantifying activity and/or infiltration of one or more immune cell in the tumor tissue. In some examples, at least one of the plurality of assays comprises quantifying activity and/or infiltration of T cells in the tumor tissue. In some examples, the T cells are cytotoxic T cells. In some examples, at least one of the plurality of assays comprises quantifying activity and/or infiltration of NK cells in the tumor tissue. In some examples, at least one

of the plurality of assays comprises quantifying the expression of one or more cytokines in the tumor tissue culture.

[0021] In some examples, according to any of the methods described above, the tumor microenvironment platform comprises an extracellular matrix composition comprising culture medium and one or more of collagen 1, collagen 3, collagen 4, collagen 6, Fibronectin, Vitronectin, Cadherin, Filamin A, Vimentin, Osteopontin, Laminin, Decorin, Tenascin C, Basement membrane proteins, Cytoskeletal proteins and Matrix proteins. In some examples, the tumor microenvironment platform further comprises serum, plasma, or autologous peripheral blood nuclear cells (PBNC).

[0022] In some examples, according to any of the methods described above, step a) further comprises culturing tumor tissue obtained from the individual with the tumor microenvironment platform and adding the therapeutic agent to the tumor microenvironment platform. In some examples, step a) further comprises conducting the plurality of assays on the tumor tissue culture to generate assessment scores, thereby producing the readout. In some examples, step b) further comprises multiplying the assessment score of each of the plurality of assays with a weightage score for the assay to obtain a weighted assay score for each of the plurality of assays; and combining the weighted assay scores for each of the plurality of assays to obtain the sensitivity index.

[0023] In some examples, according to any of the methods described above, the sensitivity index predicts complete clinical response, partial clinical response, or no clinical response to the therapeutic agent in the individual.

[0024] In some examples, according to any of the methods described above, the therapeutic agent is a chemotherapeutic agent or an immunotherapeutic agent.

[0025] In some examples, according to any of the methods described above, the plurality of assays is selected from the group consisting of cell viability assays, cell death assays, cell proliferation assays, tumor morphology assays, tumor stroma content assays, cell metabolism assays, senescence assays, cytokine profile assays, enzyme activity assays, tumor and/or stromal cell expression assays, immune contexture assays, and any combination thereof.

[0026] In some examples, there is provided a method of treating cancer in an individual in need thereof, the method comprising administering to the individual a therapeutic agent having a sensitivity index according to any of the methods described above that predicts responsiveness.

[0027] In some examples, according to any of the method of treating cancer described above, the therapeutic agent has a sensitivity index that predicts complete clinical response or partial clinical response in the individual.

[0028] In some examples, according to any of the methods described above, the therapeutic agent is an immune checkpoint inhibitor. In some examples, the immune checkpoint inhibitor is an antagonistic antibody targeting an immune checkpoint molecule. In some examples, the immune checkpoint inhibitor is pembrolizumab or nivolumab.

[0029] In some examples, according to any of the methods described above, the plurality of therapeutic agents comprises a plurality of immune checkpoint inhibitors. In some examples, the plurality of immune checkpoint inhibitors comprises a plurality of antagonistic antibodies targeting an immune checkpoint molecule. In some examples, the plurality of immune checkpoint inhibitors comprises pembrolizumab and nivolumab.

[0030] In some examples, according to any of the methods described above, the individual is human.

BREIF DESCRIPTION OF THE DRAWINGS

[0031] FIG. 1 shows results for H&E staining and IHC analysis for cleaved caspase 3, MICA/B, and CD56 expression in tumor tissue cultured in the tumor microenvironment platform treated with gefitinib, osimertinib + Pembrolizumab, or vehicle control for 3 days (T3).

[0032] FIGS. 2A-2C show NK cell spatial heterogeneity in tissue cultured in the tumor microenvironment platform treated with various conventional and immuno-modulatory therapies. FIG. 2A shows IHC analysis for NK cell marker CD56 under treatment and control conditions. Areas of tumor cells (T), normal stroma (S), and normal cells (N) are indicated. FIG. 2B shows pairwise quantitation of the ratio of CD56+ cells in areas of tumor cells vs areas of stroma in untreated (Vehicle) and drug pressure (Rx) conditions. FIG. 2C shows the fold change in the CD56+ tumor:stroma ratio from untreated to drug pressure conditions.

[0033] FIGS. 3A and 3B show changes in NK cell spatial heterogeneity in tissue cultured in the tumor microenvironment platform under pressure from treatment with immunotherapy-containing drug regimens (Rx) nivolumab + adriamycin (FIG. 3A) and gemcitabine + nivolumab + ipilimumab (FIG. 3B) as compared to vehicle control (Vehicle). Areas of tumor cells (T) and normal stroma (S) are indicated.

[0034] FIG. 4 shows changes in NK cell spatial heterogeneity in tissue cultured in the tumor microenvironment platform under pressure from treatment with anticancer drug

CLAIMS

1. A method of predicting responsiveness of an individual having a cancer to administration of an anticancer drug regimen, the method comprising:

a) obtaining a readout comprising an assessment score for each of a plurality of assays conducted on a tumor tissue culture treated with the anticancer drug regimen, wherein the tumor tissue culture comprises a tumor tissue from the individual cultured on a tumor microenvironment platform, and

wherein the plurality of assays comprises a first set of a plurality of assays and a second set of one or more assays, wherein the second set of one or more assays comprises determining i) an amount of an immune cell in a region of tumor cells in the tumor tissue culture and ii) an amount of the immune cell in a region of normal stroma in the tumor tissue culture;

b) inputting the readout into a predictive model;

c) using the predictive model to generate an output; and

d) using the output to predict responsiveness of the individual to administration of the anticancer drug regimen.

2. A method of classifying likely responsiveness of an individual having a cancer to administration of an anticancer drug regimen, comprising:

a) obtaining a readout comprising an assessment score for each of a plurality of assays conducted on a tumor tissue culture treated with the anticancer drug regimen,

wherein the tumor tissue culture comprises a tumor tissue from the individual cultured on a tumor microenvironment platform, and

wherein the plurality of assays comprises a first set of a plurality of assays and a second set of one or more assays, wherein the second set of one or more assays comprises determining i) an amount of an immune cell in a region of tumor cells in the tumor tissue culture and ii) an amount of the immune cell in a region of normal stroma in the tumor tissue culture;

b) inputting the readout into a predictive model;

c) using the predictive model to generate an output; and

d) using the output to classify the likely responsiveness of the individual to administration of the anticancer drug regimen.

3. A computer-implemented method for predicting responsiveness of an individual having a cancer to administration of an anticancer drug regimen, the method comprising:

a) accessing a readout comprising an assessment score for each of a plurality of assays conducted on a tumor tissue culture treated with the anticancer drug regimen,

wherein the tumor tissue culture comprises a tumor tissue from the individual cultured on a tumor microenvironment platform, and

wherein the plurality of assays comprises a first set of a plurality of assays and a second set of one or more assays, wherein the second set of one or more assays comprises determining i) an amount of an immune cell in a region of tumor cells in the tumor tissue culture and ii) an amount of the immune cell in a region of normal stroma in the tumor tissue culture;

b) inputting the readout into a predictive model;

c) using the predictive model to generate an output; and

d) using the output to predict responsiveness of the individual to administration of the anticancer drug regimen.

4. The method of any one of claims 1-3, wherein the predictive model comprises a first algorithm that uses each of the assessment scores as input and generates the output.

5. The method of claim 4, wherein the first algorithm comprises multiplying each of the input assessment scores with a corresponding weightage coefficient to obtain a plurality of weighted assessment scores; and combining the plurality of weighted assessment scores to generate the output.

6. The method of any one of claims 1-3, wherein the predictive model comprises i) a first algorithm that uses each of the assessment scores for the first set of a plurality of assays as input and generates a preliminary output, and ii) a second algorithm that uses the preliminary output and each of the assessment scores for the second set of one or more assays as input and generates the output.

7. The method of claim 6, wherein the first algorithm comprises i) multiplying each of the assessment scores for the first set of the plurality of assays with a corresponding weightage

coefficient to obtain a plurality of weighted assessment scores; and ii) combining the plurality of weighted assessment scores to generate the preliminary output.

8. The method of claim 6 or 7, wherein the preliminary output predicts a primary degree of responsiveness of the individual to administration of the anticancer drug regimen, and wherein the second algorithm comprises adjusting the primary degree of responsiveness based on the assessment scores from the second set of one or more assays to generate the output.

9. The method of claim 8, wherein adjusting the primary degree of responsiveness comprises:
1) decreasing the primary degree of responsiveness if the assessment scores from the second set of one or more assays is below a first threshold, thereby generating the output ; or
2) increasing the primary degree of responsiveness if the assessment scores from the second set of one or more assays is above a second threshold, thereby generating the output.

10. The method of any one of claims 1-9, wherein the output predicts complete clinical response, partial clinical response, or no clinical response of the individual to administration of the anticancer drug regimen.

11. The method of any one of claims 1-9, wherein the output predicts response or no response of the individual to administration of the anticancer drug regimen.

12. The method of any one of claims 1-11, wherein the second set of one or more assays comprises determining a ratio of i) an amount of an immune cell in a region of tumor cells in the tumor tissue culture to ii) an amount of the immune cell in a region of normal stroma in the tumor tissue culture.

13. The method of any one of claims 1-12, wherein the immune cell is a natural killer cell.

14. The method of any one of claims 1-13, wherein the immune cell is a CD56+ cell.

15. The method of any one of claims 1-14, wherein the first set of a plurality of assays is selected from the group consisting of cell viability assays, cell death assays, cell proliferation

assays, tumor morphology assays, tumor stroma content assays, cell metabolism assays, senescence assays, cytokine profile assays, enzyme activity assays, tumor: stromal cell expression assays, and any combination thereof.

16. The method of any one of claims 1-15, wherein the tumor microenvironment platform comprises an extracellular matrix composition comprising one or more of collagen 1, collagen 3, collagen 4, collagen 6, Fibronectin, Vitronectin, Cadherin, Filamin A, Vimentin, Osteopontin, Laminin, Decorin, and Tenascin C.

17. The method of any one of claims 1-16, wherein the tumor microenvironment platform comprises one or more of serum, plasma, and peripheral blood nuclear cells (PBNCs).

18. The method of claim 17, wherein one or more of the serum, plasma, and PBNCs are derived from the individual.

19. The method of any one of claims 1-18, wherein the assessment scores are generated based on a comparison between i) the results of the plurality of assays conducted on the tumor tissue culture treated with the anticancer drug regimen; and ii) the results of the plurality of assays conducted on a reference tumor tissue culture, wherein the reference tumor tissue culture comprises a tumor tissue from the individual cultured on the tumor microenvironment platform, and wherein the reference tumor tissue culture is not treated with the anticancer drug regimen.

20. Use of an anticancer drug regimen to which the individual is predicted to respond according to the method of any one of claims 1-19 in the manufacture of a medicament for treating cancer in an individual in need thereof.

21. The method of any one of claims 1-19 or the use of claim 20, wherein the of the anticancer drug regimen is selected from a group consisting of a chemotherapeutic agent, a targeted therapeutic agent, an immunotherapeutic agent, and any combination thereof.

22. The use of claim 20, wherein the immunotherapeutic agent is an immune checkpoint inhibitor.

23. The use of claim 22, wherein the immunotherapeutic agent is selected from the group consisting of nivolumab, ipilimumab, pembrolizumab, atezolizumab, and any combination thereof.
24. The method of any one of claims 1-19 or the use of any one of claims 20-23, wherein the individual is human.
25. A method comprising :
- a) culturing a tumor tissue obtained from an individual on a tumor microenvironment platform to obtain a tumor tissue culture,
 - b) conducting an assay on the tumor tissue culture treated with an anticancer drug regimen; wherein the assay comprises determining i) an amount of an immune cell in a region of tumor cells in the tumor tissue culture and ii) an amount of the immune cell in a region of normal stroma in the tumor tissue culture.
26. The method of claim 25, further comprising the step of generating an assessment score for the assay.
27. The method of claim 26, further comprising the step of using the assessment score to predict responsiveness of the individual to administration of the anticancer drug regimen.
28. The method of claim 25, wherein said determining in step (b) comprises determining a ratio of i) an amount of an immune cell in a region of tumor cells in the tumor tissue culture to ii) an amount of the immune cell in a region of normal stroma in the tumor tissue culture.
29. The method of claim 25, wherein the immune cell is a natural killer cell.
30. The method of claim 25, wherein the immune cell is a CD56+ cell.
31. The method of claim 25, further comprising:

a) conducting one or more additional assays on the tumor tissue culture treated with the anticancer drug regimen,

wherein the one or more additional assays is selected from a group consisting of a cell viability assay, a cell death assay, a cell proliferation assay, a tumor morphology assay, a tumor stroma content assay, a cell metabolism assay, a senescence assay, a cytokine profile assay, an enzyme activity assay, a tumor: stromal cell expression, and any combination thereof; and

b) generating an assessment score for each assay in the one or more additional assays.

32. The method of claim 31, further comprising:

a) multiplying each assessment score with a corresponding weightage coefficient to obtain a plurality of weighted assessment scores;

b) combining the plurality of weighted assessment scores to generate an output; and

c) using the output to predict responsiveness of the individual to administration of the anticancer drug regimen.

33. The method of claim 25, wherein the tumor microenvironment platform comprises an extracellular matrix composition comprising one or more of collagen 1, collagen 3, collagen 4, collagen 6, Fibronectin, Vitronectin, Cadherin, Filamin A, Vimentin, Osteopontin, Laminin, Decorin, and Tenascin C.

34. The method of claim 25, wherein the anticancer drug regimen is selected from a group consisting of a chemotherapeutic agent, a targeted therapeutic agent, an immunotherapeutic agent, and any combination thereof.

35. The method of claim 25, wherein the tumor microenvironment platform comprises one or more of serum, plasma, and peripheral blood nuclear cells (PBNCs).

36. The method of claim 25, wherein one or more of the serum, plasma, and PBNCs are derived from the individual.