CLAIMS

~~What is claimed is:~~

1. A method of evaluating the ability of an anti-cancer drug candidate to induce apoptosis in a cancer cell line derived from a tumor specimen, comprising:

a) obtaining a tumor specimen;

b) mincing, digesting, and filtering the specimen to produce a cell suspension;

c) optionally removing non-viable cells by density gradient centrifugation;

d) incubating the cell suspension to remove macrophages by adherence;

e) performing positive and/or negative isolation to isolate the cells of interest; including optionally removing remaining macrophages using CD 14 antibody conjugated magnetic beads, to produce a final suspension;

f) plating cells from the final suspension into wells of a plate;

g) incubating the plate;

h) exposing at least one well of a plated final suspension to at least one anti-cancer drug candidate or mixtures of the candidate and other substances;

i) measuring the optical density of the wells exposed to the at least one anti-cancer drug candidates, or wells containing mixtures of at least one anti-cancer drug candidate and other substances, wherein said measuring of the optical density occurs in a serial manner at selected time intervals for a selected duration of time;

j) determining a kinetic units value for the at least one anti-cancer drug candidates from the optical density and time measurements using a Coefficient value between 0.8 and 1.5 that is determined for the wells using the formula:

$$\text{Coefficient} = X/(OD_{control} - OD_{blank}), \text{ wherein}$$

X = optimal optical density for a cell type being tested,

$OD_{control}$ = average optical density of all control wells, and

OD_{blank} = average optical density of all blank wells;

k) correlating the kinetic units value for each drug candidate with:

a) an ability of the anti-cancer drug candidate to induce apoptosis in the cancer cells if the kinetic units value is greater than a predetermined threshold; or

b) an inability of the anti-cancer drug candidate to induce apoptosis in the cancer cells if the kinetic units value is less than a predetermined threshold.

~~1~~2. A method of evaluating the relative apoptosis-inducing activity of an anti-cancer drug candidate, comprising:

a) obtaining ~~cancer cells from~~ a tumor specimen;

b) mincing, digesting, and filtering the specimen to produce a cell suspension;

c) optionally removing non-viable cells by density gradient centrifugation;

d) incubating the cell suspension to remove macrophages by adherence;

e) performing positive and/or, negative~~, and/or depletion~~ isolation to isolate ~~the~~ cancer cells of interest; including optionally

f) removing any remaining macrophages, if necessary, using CD 14 antibody conjugated magnetic beads, to produce a final suspension;

fg) plating cells from the final suspension into wells of a plate;

gh) incubating the plate;

hi) exposing at least one well of a plated final suspension to at least one first anti-cancer drug candidate or mixtures of the first candidate and other substances;

ij) exposing at least one well of a plated final suspension to at least one second anti-cancer drug candidate or mixtures of the second candidate and other substances;

jk) measuring the optical density of the wells exposed to the at least one first and second anti-cancer drug candidates, or wells containing mixtures of at least one first or at least one second anti-cancer drug candidate and other substances, wherein said measuring of the optical density occurs in a serial manner at selected time intervals for a selected duration of time;

kl) determining a kinetic units value for the at least one first and second anti-cancer drug candidates from the optical density and time measurements using a Coefficient value between 0.8 and 1.5 that is determined for the wells using the formula:

$$\text{Coefficient} = X/(OD_{control} - OD_{blank}), \text{ wherein}$$

X = optimal optical density for a cell type being tested,

$OD_{control}$ = average optical density of all control wells, and

OD_{blank} = average optical density of all blank wells;

lm) correlating the kinetic units value for each drug candidate with:

a) an ability of the anti-cancer drug candidate to induce apoptosis in the cancer cells if the kinetic units value is greater than a predetermined threshold; or

b) an inability of the anti-cancer drug candidate to induce apoptosis in the cancer cells if the kinetic units value is less than a predetermined threshold;

mn) comparing the determined kinetics units value for each drug candidate; and

no) determining a drug candidate that has a greater relative ability to induce apoptosis in a the cancer cell based upon the comparison in step (mn).

23. The method of claim 12, wherein the at least one first and second anti-cancer drug candidates comprise at least one generic drug candidate and one proprietary drug candidate.

34. The method of claim 23, further comprising the step of:

po) determining the monetary consequences resultant from choosing either the generic or proprietary drug candidate, wherein the drug candidate with the highest relative kinetic units value is selected.

4. The method of claim 3, , optionally wherein the monetary consequences are determined based upon treating a single patient with the selected drug with the higher kinetic units value versus the cost that would have occurred based upon the drug candidate with the lower kinetic units value.

5. The method of claim 34, further comprising the step of:

qp) extrapolating the monetary consequences determined from step qo) to a target population.

6. The method of claim 5, , optionally wherein the target population is a nationwide population from the United States.

67. The method of claim 34, wherein the monetary consequences of step po) are determined by a method comprising:

i) obtaining Medicare cost payment schedules for the selected anti-cancer drug with the higher kinetic units value and also for the drug with the lower kinetic units value;

ii) determining the relative monetary cost savings or relative monetary expenditure that would accrue to a single patient based upon treating said patient with the drug candidate with the higher relative kinetic units value versus treating said patient with the drug candidate with the lower kinetic units value, wherein said treatment comprises at least one cycle of treatment with the selected anti-cancer drug candidate; and

iii) extrapolating the cost savings or relative monetary expenditure from step ii) out to a target population of interest.

~~8. The method of claim 1, wherein the tumor specimen is a solid tumor specimen, or a blood specimen, or a bone marrow specimen, or an effusion derived specimen.~~

~~7~~9. The method of claim ~~1~~2, wherein at least one of the first or second anti-cancer drug candidates is a combination comprising said anti-cancer drug candidate and at least one additional anti-cancer drug candidate.

~~10. The method of claim 1, wherein each well of the plate comprises a different anti-cancer drug candidate.~~

~~11. The method of claim 1, wherein each well of the plate comprises a different concentration of the anti-cancer drag candidate.~~

~~12. The method of claim 1, wherein the anti-cancer drug candidate concentration is from 0.01 to 10,000μM.~~

~~13. The method of claim 1, wherein the optical density is serially measured and recorded approximately every 5 minutes for a period of approximately 48 hours.~~

~~14. The method of claim 1, wherein the optical density is measured by a spectrophotometer at a wavelength of from 550 to 650 nanometers.~~

~~15. The method of claim 1, wherein the at least one anti-cancer drug candidates are selected from the group consisting of: Abraxane, Alimta, Amsacrine, Asparaginase, Bendamustine, Bleomycin, Bosutinib, Caelyx (Doxil), Carboplatin, Carmustine, CCNU, Chlorambucil, Cisplatin, Cladribine, Clofarahine, Cytarabine, Cytoxan (4HC), Dacarbazine, Dactinomycin, Dasatinib, Daunorubicin, Decitabine, Dexamethasone, Docetaxel, Doxorubicin, Epirubicin, Eribulin, Erlotinib, Estramustine, Etoposide, Everolimus, Fludarabine, 5-Fluorouracil, Gemcitabine, Gleevec (imatinib), Hydroxyurea, Idarabicin, Ifosfamide (4HI), Interferon-2a, Irinotecan, Ixabepilone, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitoxantrone, Nilotinib, Nitrogen Mustard, Oxaliplatin, Paclitaxel, Pentostatin, Procarbazine, Regorafenib,~~

~~Sorafenib, Streptozocin, Sunitinib, Temozolomide, Temsirolimus, Teniposide, Thalidomide, Thioguanine, Topotecan, Velcade, Vidaza, Vinblastine, Vincristine, Vinorelbine, Vorinostat, Everolimus, Lapatinib, Lenalidomide, Rapamycin, and Votrient (Pazopanib).~~

~~8~~16. The method of claim ~~2~~3, wherein the at least one anti-cancer generic drug candidates are selected from the group consisting of: cyclophosphamide, doxorubicin, epirubicin, paclitaxel, docetaxel, cisplatin, carboplatin, irinotecan, topotecan, vinorelbine, and vinblastine.

~~17~~9. The method of claim ~~2~~3, wherein the at least one anti-cancer proprietary drug candidates are selected from the group consisting of: nab-paclitaxel, gemcitabine, oxaliplatin, capcitabine, ixabepilone, erubilin, liposomal doxorubicin, and pemetrexed.

~~18. A method of tumor cell isolation and purification, comprising:~~
~~a) obtaining a tumor specimen;~~
~~b) mincing, digesting, and filtering the specimen;~~
~~c) optionally removing non-viable cells by density gradient centrifugation;~~
~~d) incubating the cell suspension to remove macrophages by adherence;~~
~~e) performing positive, negative, and/or depletion isolation to isolate the cells of interest;~~
~~f) removing any remaining macrophages, if necessary, using CD14 antibody conjugated magnetic beads;~~
~~g) plating the final suspension; and~~
~~h) incubating the plate.~~

~~19. A method of evaluating the ability of an anti-cancer drug candidate to induce apoptosis in a cancer cell line derived from a tumor specimen, comprising:~~
~~a) obtaining a tumor specimen;~~
~~b) mincing, digesting, and filtering the specimen;~~
~~c) optionally removing non-viable cells by density gradient centrifugation;~~
~~d) incubating the cell suspension to remove macrophages by adherence;~~
~~e) performing positive, negative, and/or depletion isolation to isolate the cells of interest;~~

~~f) removing any remaining macrophages, if necessary, using CD 14 antibody conjugated magnetic beads;~~

~~g) plating the final suspension;~~

~~h) incubating the plate;~~

~~i) exposing at least one well of a plated final suspension to at least one anti-cancer drug candidate or mixtures of the candidate and other substances;~~

~~j) measuring the optical density of the wells exposed to the at least one anti-cancer drug candidate, or wells containing mixtures of at least one anti-cancer drug candidate and other substances, wherein said measuring of the optical density occurs in a serial manner at selected time intervals for a selected duration of time;~~

~~k) determining a kinetic units value for the at least one anti-cancer drug candidate from the optical density and time measurements; and~~

~~l) correlating the kinetic units value for each drug candidate with:~~

~~a) an ability of the anti-cancer drug candidate to induce apoptosis in the cancer cells if the kinetic units value is greater than a predetermined threshold;~~

~~b) an inability of the anti-cancer drug candidate to induce apoptosis in the cancer cells if the kinetic units value is less than a predetermined threshold.~~

10~~20~~. The method of claim 1 or 2~~19~~, wherein each well of the plate comprises a different anti-cancer drug candidate~~,~~

~~21. The method of claim 19,~~or ~~wherein~~ each well of the plate comprises a different concentration of the anti-cancer drug candidate.

11~~22~~. The method of claim 1 or 2~~19~~, wherein the anti-cancer drug candidate concentration is from 0.01 to 10,000 µM.

12~~23~~. The method of claim 1 or 2~~19~~, wherein the optical density is serially measured and recorded approximately every 5 minutes for a period of approximately 48 hours.

13~~24~~. The method of claim 1 or 2~~19~~, wherein the optical density is measured by a spectrophotometer at a wavelength of from 550 to 650 nanometers.

1425. The method of claim 1 or 249, wherein the tumor specimen is a solid tumor specimen, or a blood specimen, or a bone marrow specimen, or an effusion derived specimen.

1526. The method of claim 1 or 2 ~~19~~, wherein the anti-cancer drug candidates are selected from the group consisting of: Abraxane, Alimta, Amsacrine, Asparaginase, Bendamustine, Bleomycin, Bosutinib, Caelyx (Doxil), Carboplatin, Carmustine, CCNU, Chlorambucil, Cisplatin, Cladribine, Clofarabine, Cytarabine, Cytoxan (4HC), Dacarbazine, Dactinomycin, Dasatinib, Daunorubicin, Decitabine, Dexamethasone, Docetaxel, Doxorubicin, Epirubicin, Eribulin, Erlotinib, Estramustine, Etoposide, Everolimus, Fludarabine, 5-Fluorouracil, Gemcitabine, Gleevec (imatinib), Hydroxyurea, Idarubicin, Ifosfamide (4HI), Interferon-2a, Irinotecan, Ixabepilone, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitoxantrone, Nilotinib, Nitrogen Mustard, Oxaliplatin, Paclitaxel, Pentostatin, Procarbazine, Regorafenib, Sorafenib, Streptozocin, Sunitinib, Temozolomide, Temsirolimus, Teniposide, Thalidomide, Thioguanine, Topotecan, Velcade, Vidaza, Vinblastine, Vincristine, Vinorelbine, Vorinostat, Everolimus, Lapatinib, Lenalidomide, Rapamycin, and Votrient (Pazopanib).