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(54) Titre : METHODE EXHAUSTIVE DE CANCEROLOGIE POUR IDENTIFIER DES MODELES DE PROTEINE DE CANCER ET DETERMINATION DE STRATEGIES DE THERAPIE DU CANCER

(54) Title: CANCER COMPREHENSIVE METHOD FOR IDENTIFYING CANCER PROTEIN PATTERNS AND DETERMINATION OF CANCER TREATMENT STRATEGIES

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A cancer therapy comprehensive method for characterizing a cancer tumor for medical diagnosis and treatment. The method facilitates determination of a cancer protein pattern based on detected nonbasal levels of biomolecular markers (BMMs) associated with a patient's tumor. A cancer therapy regimen is selected based on the cancer protein pattern for eradicating the tumor.

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CANCER COMPREHENSIVE METHOD FOR IDENTIFYING CANCER PROTEIN PATTERNS AND DETERMINATION OF CANCER TREATMENT STRATEGIES

BACKGROUND OF THE INVENTION

5 1. Field of the Invention

The present invention relates to the detection and treatment of cancer. More particularly, the invention concerns a comprehensive method for identifying a cancer protein pattern and determining a course of chemotherapy and/or radiotherapy.

10 2. Description of Prior Art

By way of background, cancer patients are generally treated by standard and generic protocols, with the type of protocol being largely determined according to the tumor's generic histologically determined stage (determined through biopsy and tumor marker testing), and the individual clinician's experience and preference. This form of treatment is based on 15 statistical information derived from historical data and is not individualized to the specific patient. Based on microscopic examination, tumors of the same type appear very similar. However, tumors within a given patient may demonstrate divergent growth curves and characteristics as well as disparate responses to chemoregimens due to biochemical and genetic nonequivalence. Thus, it cannot be said that every and all patients exhibiting the 20 identical microscopic narrative, and hence the same stage, will respond favorably to the exact same empiric "cure-one-cure-all" therapy.

In an effort to individualize cancer therapy, a clinician may have in-vitro testing performed to pre-determine the effects of chemotherapeutic agents on tumor cells obtained from the patient. According to the usual technique, patient tumor cells are allowed to grow 25 and then tested only for resistance to cancer treatment drugs. A drug determined to be ineffective relative to the in-vitro testing may then be eliminated as the drug of choice for the patient.

There are multiple reasons why this approach may not be effective. First, because the tested tumors are grown in a culture, they represent a homogenous cell population. The 30 patient's actual tumor is typically composed of multiple diverse cell populations in varying stages of cell cycle, and expressing various extracellular, cytoplasmic, and nuclear antigens in varying concentrations, as well as containing normal stromal cells, epithelial populations and vascular endothelial cell populations. Second, by the time the in-vitro tumor has been grown

out and tested, first line chemotherapy cannot be realized due to the time needed for cellular growth (assuming the tumor grows at all). This mandates second line regimes. Moreover, when the tumor is exposed to a first line regimen that may not work, the tumor is given enough time to assemble a "blue print" in which to manufacture multi-drug resistance proteins to fight any drug regimen to which it may be subsequently exposed. Third, the drugs tested in-vitro are used at overtly high concentrations that are not physiologically achievable in-vivo. Unfortunately, the use of higher than peak plasma concentrations of drug can overwhelm the cell's infrastructure. This may "confuse" a cancer cell so that it doesn't know whether to obey its innate signal to thrive and grow or obey the extra cellular drug signal to cease growth and die. Thus, the cell merely waits for a ratiocinate signal. By the time this equilibrium is reached, the body has excreted the drug and the cell "awakens" to follow its innate signal to thrive and grow. Moreover, this "conditioning" has now allowed the cell to manufacture weapons to fight the next round of death signals (drugs). As indicated above, such weapons include multi-drug resistant proteins that pump the drug out of its intracellular milieu and into the external environment. Thus, the cell becomes drug savvy and therefore impervious to the assault. Fourth, individualized in-vitro testing is premised on the use of a single chemotherapeutic agent and is unable to evaluate the effects of combinations of agents. Applicant submits that a multi-parametered tumor must be combated with a multiplicity of agents if the tumor is to be eradicated.

Accordingly, an improvement for determining cancer chemotherapy and radiotherapy is needed. What is specifically required is a diagnostic technique that is directed to a given cancer patient and considers the gross tumor cellular content as well as molecules that characterize the tumor milieu, thereby allowing a patient's progress to be followed and ensuring that the therapy is or is not efficacious.

SUMMARY OF THE INVENTION

The foregoing problem is solved and an advance in the art is provided by a novel cancer comprehensive method in which oncolytic product selection and dosing (as well as radiotherapies) are determined through identification of a patient's individualized cancer protein pattern of physiologically present biomolecular markers and the up or down regulation of some of these markers from basal levels. In preferred implementations of the invention, the cancer protein pattern is determined from an assay evaluation sample obtained from the patient. The assay evaluation sample can be a homogenate of a solid tumor sample obtained from the patient or a blood serum/plasma sample obtained from the patient. The cancer protein pattern is based on detected nonbasal levels of biomolecular markers (BMMs)

associated with the patient's tumor. The cancer therapy regimen is then selected based on the cancer protein pattern and a first line therapy regimen is customized based on expressed BMMs in the cancer protein pattern that are above or below basal levels. The BMMs preferentially include proteins that can be modulated by protein modulating drugs and the cancer therapy regimen preferentially includes protein modulating drugs corresponding to one or more of the BMMs. The protein modulating drugs are selectively combined into a chemo-suite that directly corresponds to the BMM pattern. The BMMs may be divided into Class I BMMs representing either tumor promoting or tumor suppressor proteins and Class II BMMs representing tumor marker proteins that provide information about cancer onset and/or progression. The cancer therapy regimen can be selected by evaluating the Class I BMMs for upregulation or downregulation and evaluating the Class II BMMs if any of the Class I BMMs are determined to be upregulated or downregulated. If only one Class I BMM is upregulated or downregulated, the patient may be designated as being possibly precancerous. If only two Class I BMMs are upregulated or downregulated, the patient may be designated as being precancerous. If three or more Class I BMMs are upregulated or downregulated, the patient may be designated as being cancerous.

It is therefore an object of the invention to target cancer therapy to a specific cancer patient so that the patient's tumor is not exposed to an inappropriate regimen of drugs, thereby increasing efficacy.

Another object of the invention is to examine the heterogeneity of an entire tumor, thereby taking into consideration every cell that composes the tumor and not just those that are in DNA synthesis.

A further object of the invention is to evaluate an individual cancer patient and not use a generic treatment that is empirically and generically chosen merely based on staging for a specific cancer.

A further object of the invention is to target first-line chemotherapy.

A further object of the invention is to predetermine if radiotherapy will be effective, partially effective or not effective at all in cancer patients. This rationale is based on the fact that, like chemotherapy, radiotherapy is also chosen based on morphological characteristics and not individualized based on the specific patient's tumor heterogenic cell population characteristics.

A further object of the invention is to be able to follow and monitor a specific patient to ensure that chemotherapy or radiotherapy has been efficacious.

A further object of the invention is to be able to determine if previously treated patient in remission is at risk for recurrence, relapse or metastasis.

A further object of the invention is to be able to screen for the possible onset of cancer using the disclosed methodology during routine physical examination.

5 BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing and other features and advantages of the invention will be apparent from the following more particular description of preferred embodiments of the invention, as illustrated in the accompanying Drawings in which:

Fig. 1 is a plan view of an exemplary assay kit for use in accordance with the method

10 of the invention;

Figs. 2A –2F are diagrammatic views showing exemplary assay steps performed in accordance with the method of the invention; and

Figs. 3 is a diagrammatic plan view of showing how individual test wells may be used in the assay kit of Fig. 1.

15 DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Applicant has observed that cancer treatment evaluation must be individualized based on the patient's heterogeneous tumor cell populations. A course of treatment cannot be determined merely by morphological characteristics (staging) alone insofar as the biochemical and genetic parameters are not reflected morphologically. The invention thus

20 proposes that cancer therapy be based on tumor biomolecular (biochemical/genetic) characteristics and not merely on staging. This is accomplished by evaluating the totality of a patient's tumor cell populations (without having to grow out a tumor in-vitro) based on a plurality of the specific individual's tumor parameters to determine the chemotherapy and/or radiotherapy regimen needed to eradicate the entire tumor mass. This evaluation is

25 performed within the time constraints necessary for targeting first line treatment regimens, thereby lessening the chance that any cells will escape the "combatant" regimen while realizing few or no side effects by the patient.

The method of the invention can realize results within 24-48 hours. According to the method, a biomolecular profile is performed relative to a patient's own cancer protein pattern

30 of biomolecular markers (BMMs). The BMMs can be antigens or antibodies (proteins), such as specific tumor receptors, growth factor receptors, basement membrane components, adhesion molecules or angiogenesis components. One example is VEGF (vascular endothelial growth factor) receptor. An adult normally never vascularizes unless there is a pathological condition. This could include wound healing and in the female, normal menses

or pregnancy, but is also associated with a growing tumor. To progress beyond 3mm in size, a tumor must become invested with vessels in order to get rid of toxins and take in nutrients. The tumor will thus have an abundance of VEGF receptors so that it can derive stimulus from growth factor molecules in the circulating blood.

5 More generally, the method of the invention evaluates two classes of BMMs associated with cancer patients. The first BMM class consists of proteins (Class I BMMs) that can be targeted for treatment by way of modulating drugs that regulate (e.g., "cap") the targeted protein (e.g., signal transduction pathway (STP) monoclonal antibody drugs). Exemplary Class I BMMs include estrogen receptors (ER), progesterone receptors (PR),
10 androgen receptors (AR), and epidermal growth factor (EGFR). The second BMM class consists of proteins (Class II BMMs) that provide information about a patient's overall cancer process, such as tumor markers that may indicate cancer onset, progression and regression. Examples include cancer antigen 125 (CA-125), cancer antigen 19.9 (CA19.9), CU-18 breast related antigen, S-100, DF-3 blood factor, tumor suppressor protein p53 and c-myc oncogene.
15 Note that some proteins fall into both classes. Examples include Her2/neu growth factor receptors, multidrug resistance proteins (MRP), lung resistance proteins (LRP), proliferating cell nuclear antigen (PCNA) and urokinase plasminogen activator (uPA).

Procedure

Initially, a tumor sample is obtained from the patient and homogenated into a
20 liquefied state. The homogenate of the solid tumor will contain the cellular components that can be retrieved and used (with dilution) as an assay evaluation sample. If needed, the assay evaluation sample can be further diluted to allow evaluation of a multiplicity of BMMs (merely multiply the obtained result by the dilution factor to obtain the actual result). Blood serum/plasma may also be used to provide the assay evaluation sample insofar as the
25 circulatory system contains proteins shed by the solid tumor. Alternatively, other body fluids, such as saliva, could be obtained from the patient to provide the assay evaluation sample.

The assay evaluation sample is tagged with labeled detection antibodies or antigens that have been fluorinated or otherwise rendered detectable. Each detection antibody/antigen
30 is selected to bind to a selected Class I or Class II BMM that is considered indicative of a characteristic of the patient's tumor, with the Class I BMMs targeting proteins treatable with modulating drugs, and the Class II BMMs providing process information such as the type of cancer, the tumor's growth stage, and the tumor's ability to resist certain chemotherapies or radiotherapies. The detection antibodies/antigens will preferably be labeled for use with an

assay methodology such as ELISA (Enzyme-Linked Immunosorbent Assay) in which fluorescence is used to detect the presence of the labeled material and thus the BMM to which it is bound. Alternatively, the detection antibodies/antigens could be labeled for detection using the laser photometrics of a flow cytometer. In addition to the detection antibodies/antigens, capture antigens/antibodies specific to the BMMs of interest are used to provide a sandwich assay format. The capture antibodies/antigens allow the BMMs to be bound to a microtiter plate or other carrier for handling.

In a preferred embodiment of the invention, and as shown in Fig. 1, a multiple test well kit 2 is provided to simultaneously test for a cancer protein pattern comprising a plurality of BMMs using ELISA evaluation. The test kit 2 is constructed using a commercially available microtiter plate 4 having an array of test wells. Fig. 1 shows a microtiter plate configured in a 96 well format, but smaller or larger sizes could be used depending on the number of BMMs to be evaluated. In the 96 well size, there are 96 separate test wells 6 arranged to provide a two dimensional array comprised of well rows 8 and well columns 10. The microtiter plate 4 is made from inert plastic or other suitable material. It can be molded as a single structure in which the test wells 6 are integrally formed together in conjunction with a surrounding frame 12. Alternatively, a strip well construction can be used in which the frame 12 is separately constructed from the test wells 6 so that the test wells can be removed from the frame. The test wells 6 that define each separate well row 8, or each separate well column 10, can then be joined together to facilitate insertion in and removal from the frame 12 as a group. If desired, the test wells 6 that comprise each well row 8 or well column 10 can be joined to each other by breakable connections so that individual test wells can be separated from the well row or well column. As described in more detail below in connection with Fig. 3, if the test wells 6 of each well column 10 are joined together, each well column 10 can be assigned for use in identifying a particular BMM of interest. Then, if the clinician does not want to look at that particular BMM, the well column 10 for that BMM can then be stripped out of the microtiter plate 4. A pertinent marker strip may be substituted if desired.

Turning now to Figs. 2A-2F, each test well 6 has a bottom surface configuration 14 that is conventionally coated with capture antigen or antibody material 16 to provide a solid phase membrane for binding target BMMs in the patient's assay evaluation sample. As is generally known, the antigen/antibody material 16 can be coated on the bottom surface 14 using a coating buffer that enhances binding. Sites that are unoccupied by the capture antigen or antibody material 16 may be blocked with a blocking buffer to prevent non-specific

binding of proteins in the assay evaluation sample, if so desired. Fig. 2A shows a test well 6 that is constructed in the foregoing manner and ready to receive an assay evaluation sample. Fig. 2B shows the same test well 6 after an assay evaluation sample obtained from a patient is placed in the well. The assay evaluation sample is assumed to contain BMMs 18 that are specific to the capture antigens or antibody material 16 bound to the well's bottom surface configuration 14. In Fig. 2C, the BMMs 18 are shown after they bind to the antigen or antibody material 16. Non-specific proteins that do not bind to the antigen or antibody material 16 are washed away. In Fig. 2D, enzyme labeled (e.g., horseradish peroxidase) detection antibodies or antigens 20 are added to the test well 6, where they bind to the captured BMMs 18. Unbound detection antibodies/antigens 20 are washed away. In Fig. 2E, a colorimetric substrate 22 (e.g., o-phenylenediamine dihydrochloride, tetramethylbenzidine (TMB)) is added to the test well 6. In Fig. 2F, the enzymes on the detection antibodies/antigens 20 cleave the substrate 22, causing a color change of the substrate solution. The intensity of the color is quantified using a spectrophotometer (e.g., ELISA reader) and is proportional to the number of target proteins in the assay evaluation sample.

As shown diagrammatically in Fig. 3, the test kit 2 is preferably configured to evaluate several BMMs in a single test, with each well column 10 being assigned to a particular BMM. In Fig. 3, there are eight well columns 10 labeled #1 through #8. Thus, eight BMMs may be tested. There are also twelve rows labeled #1 through #12. Rows #1 through #6 are used to provide standard curves to facilitate evaluation. Each well in rows #1 through #6 thus contains a sample of BMM of interest at an established concentration. Rows #7 through #9 are used to provide three different control levels, low, medium and high of the BMMs of interest. Rows #10 through #12 are used for the patient's assay evaluation samples. Three rows of samples are tested and the mean test result values are used. The various controls are assigned a specific concentration along with a standard deviation (+/-). If results fall within the designated assigned values then this indicates the curve was set up correctly and the patient results are valid.

The results of the assay test can be used to determine a course of treatment to administer to the patient. The overall methodology is to identify a cancer protein pattern of Class I BMMs based on the detected levels of these proteins. The Class I BMMs will generally be either tumor promoting proteins or tumor suppressor proteins. The assay test will identify the extent to which any tumor promoting proteins are upregulated and/or any tumor promoting proteins are downregulated. From this pattern, and with the assistance of

information provided by the presence or absence of the Class II BMMs, a chemo-regimen or radio-regimen may be targeted to maximize the eradication of the patient's solid tumor.

Most important are the Class I BMMs because they signify the presence of proteins that can be modulated by conventional STP drugs. Unlike current treatments in which one or more of such drugs are prescribed based on tumor staging, the drugs are selectively combined into a chemo-suite that directly corresponds to a specific patient's BMM pattern revealed for that patient by the assay test. The treatment is thus customized to target cells that express the BMMs represented in the pattern. The significance of the Class II BMMs can be appreciated from the fact that each of the Class I BMMs is a normally expressed antigen that may be found in non-cancerous tissue at basal levels. Even if a particular Class I BMM is above or below its basal level, it may not be appropriate to make a diagnosis of cancer. For example, most individuals do not normally express up-regulated levels of VEGF. However, as previously mentioned, an assay test of a female during normal menses or pregnancy could reveal such up-regulation. On the other hand, the additional presence of a Class II BMM such as CA-125 could lead to a different diagnosis. Similarly, elevated levels of more than one tumor promoting protein or decreased levels of more than one tumor suppressor protein could provide a more definitive diagnosis. For example, the presence of two Class I BMMs would likely be interpreted as a pre-cancerous condition. The presence of three or more Class I BMMs would likely be interpreted as cancer.

Advantageously, the method of the invention facilitates such definitive diagnoses by testing for the patient's cancer protein patterns rather than individual proteins, such as various prior art assays that identify individual tumor markers. This is particularly useful for first line chemotherapy. Rather than prescribing drugs according conventional staging methods and running the risk that the drugs will be inefficacious and promote drug resistance that impacts second line treatment, a carefully targeted treatment suite can be prescribed that the practitioner reasonably knows will control the identified BMMs.

Exemplary Test Kits

A number of basic test kit profiles have been developed to characterize different cancers. Table 1 below illustrates several exemplary profiles that respectively characterize ovarian cancer, ovarian/peritoneal cancer, and ovarian/gall bladder/peritoneal cancer. It will be seen that either a basic or comprehensive profile may be used for each cancer. A basic profile may comprise a gradient either greater than or equal to five BMMs. A comprehensive profile may comprise a gradient greater than or equal to ten BMMs. In Table 1 below, three exemplary basic profiles and three exemplary comprehensive profiles are shown. The first

two profiles are for ovarian cancer, the second two are for ovarian/peritoneal cancer, and the third two profiles are for ovarian/gall bladder/peritoneal cancer.

TABLE 1

TUMOR TYPE	BASIC PROFILE	COMP. PROFILE
OVARIAN	ER/PR, Her2/neu, MRP, LRP, EGFR	ER/PR/AR, Her2/neu, MRP, LRP, EGFR, CA-125, CU-18, PCNA, DF 3, uPA
OVARIAN/PERITONEAL	S-100, PCNA, MDR-1, EGFR, ER/PR/AR	S-100, PCNA, MDR-1, EGFR, ER/PR/AR, Ki-67, p53, Her2/neu, MRP, LRP, EGFR, CA-125, uPA
OVARIAN/GALLBLADDER/ PERITONEAL	S-100, PCNA, MDR-1, EGFR ER/PR/AR, PP, p53, c-myc	S-100, PCNA, MDR-1, EGFR ER/PR/AR, PP, MRP, S-100, NSE, LMW Keratin, p53, TS, CD43, CEA, CD31, CA 242, c-myc, PDECGF, VIP

5 Ovarian Cancer

The ovarian basic profile includes antibodies to detect for the presence of estrogen receptors (ER), progesterone receptors (PR), Her2/neu growth factor receptors, multidrug resistance proteins (MRP), lung drug resistance proteins (LRP) and epidermal growth factor receptors (EGFR). The ovarian comprehensive profile includes the same markers plus 10 markers to detect for the presence of androgen receptors (AR), CA-125 antigen, CU-18 breast-related antigen, proliferating cell nuclear antigen (PCNA), DF-3 blood factor and urokinase plasminogen activator (uPA).

The capture antibodies that may be used to detect the above-identified ovarian cancer BMMs are set forth in Table 2 below. They are all conventionally available monoclonal or 15 polyclonal antibodies with polyclonal antibodies being preferred to ensure detection of the specific proteins of interest. These proteins will be composed of multiple epitopes to which the polyclonal antibodies may bind. Monoclonal antibodies will target only one epitope and if that epitope has mutated, the monoclonal antibody will not bind. The assay would then give a false indication that the protein of interest is not present when in fact it is. Because a

polyclonal antibody targets many epitopes on the protein of interest, there is an increased chance that the protein will be detected by the assay.

TABLE 2

BMM	CAPTURE ANTIBODY
ER/PR/AR	ER/PR/AR antibody
Her2/neu	Her2/neu antibody
MRP	MRP antibody
LRP	LRP antibody
EGFR	EGFR antibody
CA-125	CA-125 antibody
CU-18	CU-18 antibody
PCNA	PCNA antibody
DF-3	DF-3 antibody
UPA	uPA antibody

5 Note that all of the above ovarian cancer BMMs except CA-125, CU-18 and DF 3 may be considered Class I BMMs. All of the BMMs except ER/PR and EGFR may also be considered Class II BMMs. Relative to the BMMs having Class I status, Table 3 below lists conventional drugs that may be used to modulate such proteins:

TABLE 3

Class One BMM	Drug
ER/PR/AR	Hormone capping antibodies
Her/neu	Herceptin
MRP	Glucosylceramide synthase antisense cDNA
LRP	Clafazimine
EGFR	ZD 1839 or vaccine
PCNA	NAMI-A (Ruthenium Complex)
UPA	WX-360 (uPAR-antagonist)

10

Ovarian/Peritoneal Cancer

The ovarian/peritoneal basic profile includes markers to detect for the presence of cancer antigen 19-9 (CA19-9), S-100, proliferating cell nuclear antigen (PCNA), multidrug resistance-1 (MDR-1), epidermal growth factor receptors (EGFR), estrogen receptors (ER),

progesterone receptors (PR) and androgen receptors (AR). The ovarian/peritoneal comprehensive profile includes the same markers plus markers to detect for the presence of monoclonal antibody Ki-67; tumor suppressor protein (p53), Her2/neu growth factor receptors, multidrug resistance proteins (MRP), lung drug resistance proteins (LRP), cancer
5 antigen 125 (CA125) and urokinase plasminogen activator (uPA).

The capture antibodies that may be used to detect the above-identified ovarian/peritoneal cancer BMMs are set forth in Table 4 below. They are all conventionally available polyclonal or monoclonal antibodies (with polyclonal antibodies being preferred), as follows:

0 TABLE 4

BMM	CAPTURE ANTIBODY
CA19-9	CA19-9 antibody
S-100	S-100 antibody
PCNA	PCNA antibody
MDR-1	MDR-1 antibody
EGFR	EGFR antibody
ER/PR/AR	ER/PR/AR antibody
Ki-67	Ki-67 antibody
p53	p53 antibody
Her2/neu	Her2/neu antibody
MRP	MRP antibody
LRP	LRP antibody
CA-125	CA-125 antibody
UPA	uPA antibody

Note that all of the above ovarian/peritoneal cancer BMMs except CA-19-9, S-100, p53 and CA-125 may be considered Class I BMMs. All of the BMMs except ER/PR/AR and EGFR may also be considered Class II BMMs. Relative to the BMMs having Class I status,
15 Table 5 below lists conventional drugs that may be used to modulate such proteins:

TABLE 5

Class One BMM	Drug
ER/PR/AR	Hormone capping antibodies
Her/neu	Herceptin

MRP	Glucosylceramide synthase antisense cDNA
LRP	Clafazimine
EGFR	ZD 1839 or vaccine
MDR-1	Taxanes
Ki-67	S-phase targeting drugs
PCNA	NAMI-A (Ruthenium Complex)
UPA	WX-360 (uPAR-antagonist)

Ovarian/Gall Bladder/Peritoneal Cancer

The ovarian/gall bladder/peritoneal basic profile includes markers to detect for the presence of cancer antigen 19-9 (CA19-9), S-100, proliferating cell nuclear antigen (PCNA), 5 MDR-1, epidermal growth factor receptors (EGFR), estrogen receptors (ER), progesterone receptors (PR), androgen receptors (AR), PP, tumor suppressor protein (p53) and c-myc. The ovarian/gall bladder/peritoneal comprehensive profile includes the same markers plus markers to detect for the presence of MRP, neuron-specific enolase (NSE), LMW Keratin, thymidylate synthase (TS), sialophorin (CD43), carcinoembryonic antigen (CEA), PECAM-1 10 (CD31), cancer antigen 242 (CA242), platelet-derived endothelial cell growth factor (PDECGF) and vasoactive intestinal peptide (VIP).

The antibodies/antigens that may be used to detect the above-identified ovarian/gall bladder/peritoneal cancer BMMs are set forth in Table 6 below. They are all conventionally available polyclonal or monoclonal antibodies (with polyclonal antibodies being preferred), 15 as follows:

TABLE 6

BMM	CAPTURE ANTIBODY
CA19-9	CA19-9 antibody
S-100	S-100 antibody
PCNA	PCNA antibody
MDR-1	MDR-1 antibody
EGFR	EGFR antibody
ER/PR/AR	ER/PR/AR antibody
PP	PP antibody
p53	p53 antibody
c-myc	c-myc antibody

MRP	MRP antibody
NSE	NSE antibody
LMW Keratin	LMW keratin antibody
TS	TS antibody
CD43	CD43 antibody
CEA	CEA antibody
CD31	CD31 antibody
CA 242	CA 242 antibody
PDECGF	PDECGF antibody
VIP	VIP polyclonal antibody

Note that all of the above ovarian/peritoneal/gall bladder cancer BMMs except CA-19-9, S-100, p53, c-myc and CA 242 may be considered Class I BMMs. All of the BMMs except ER/PR/AR and EGFR may also be considered Class II BMMs. Relative to the BMMs having Class I status, Table 7 below lists conventional drugs may be used to modulate such proteins:

TABLE 7

Class One BMM	Drug
ER/PR/AR	Hormone capping antibodies
Her/neu	Herceptin
MRP	Glucosylceramide synthase antisense cDNA
LRP	Clafazimine
EGFR	ZD 1839 or vaccine
PCNA	NAMI-A (Ruthenium Complex)
MDR-1	Taxanes
PP	Liposomal daunorubicin antisense cDNA
NSE	Cyclophosphamide, Etopaside, Soxorubicin
LMW Keratin	LMW Keratin (cytoKeratin) capping antibody
TS	Fluoropyrimidines (5-FU)
CD43	Anti CD43
CEA	Prodrug genetherapy METgene-SeMET
CD31	Anti CD31

Additional Profiles and Panels

Many other exemplary assay kit profiles and panels can be constructed in accordance with the present invention. Table 8 below shows a number of additional assay kit profiles, while Table 9 below shows a number of smaller assay kit panels for targeting specific protein groups. As explained below, many of the panels of Table 9 can be used to augment the profiles of Table 8, thereby providing additional information about patient treatment options.

TABLE 8

TUMOR TYPE	BASIC PROFILE	COMP. PROFILE
Adeno-Carcinoma	ACTH, B72.3, BCA225, Bcl-2, CA15.3	ACTH, B72.3, BCA225, Bcl-2, CA15.3, CA125, CEA/D-14, CyclinD1, PCNA, Ki-67, MRP, MDR-1 (ψ) (χ) (*f*) (λ)
Bladder	p53, Her2/neu (p185), PCNA, MDR-1, EGFR	p53, Her2/neu (p185), PCNA, MDR-1, EGFR, Ki-67, pan-ras, Bcl-2, Bcl-x, Rb (π)
Brain	p53, Her2/neu, MGMT, Ki-67, MDR-1, GFAP, Syn	p53, Her2/neu, MGMT, Ki-67, MDR-1, GFAP, Syn, CD35, CD31, PCNA, VEGFR, PDGFR (ψ) (♥) (∞)
Breast [Adeno-Carcinomas]	ER/PR, Her2/neu, TS, BCA-125, MDR-1, MRP	ER/PR, Her2/neu, TS, BCA-125, MDR-1, MRP, CA-125, p53, CD31, CA 125, DF 3, VEGFR (*) (ξ)
Colon/Bowel	p53, TS, CD43, CEA, PCNA	p53, TS, CD43, CEA, PCNA, MDR-1, CD31, CA 242, c-myc, PDECGF, VIP
Endometrial	ER/PR, Ki-67, p53, MDR-1	ER/PR, Ki-67, p53, MDR-1, CD31, CA-125, MPR, TSP, ras (ξ) (∞)
Lung	p53, LRP, NSE, MDR-1 CEA, CA-125	p53, LRP, NSE, MDR-1 CEA, CA-125, bcl-2, Cyfra 21-1, CA 19-9, MGMT, MRP (**) (ξ) (ψ)
Melanoma	MDR-1, p53, CD31, HMB-45, MRP, EGFR, Involucrin	MDR-1, p53, CD31, HMB-45, MRP, EGFR, Involucrin, Bcl-2, c-myc, PCNA, Ki67, NIKI (ψ) (λ)

Oral	p53, MDR-1, MRP, EGFR, PCNA, CA-125	p53, MDR-1, MRP, EGFR, PCNA, CA-125
Peritoneal	CA19.9, Gastrin, S-100, PCNA, NSE	CA19.9, Gastrin, S-100, PCNA, NSE, MDR, MRP, Ki-67, p53, EGFR
Prostrate	AR, HPAP, PSMA, c-erb-2, Ki-67, GRP	AR, HPAP, PSMA, c-erb-2, Ki-67, GRP, p53, MDR-1, P-cadherin, VEGF, CD31 (π)
Sarcoma	p53, MDR-1, MRP, EGFR, O13	p53, MDR-1, MRP, EGFR, O13, VEGR, Bcl-2, c-myc, PCNA, Ki-67 (ψ)
Stomach [Omentum]	CA19.9, Gastrin, PP, PCNA, MDR-1, S-100, HBP-P	CA19.9, Gastrin, PP, PCNA, MDR-1, S-100, HBP-P, NSE, LMW Keratin, Villin
Thyroid	Iodine-R, Thyro-R, TSH-R, PCNA, p53	Iodine-R, Thyro-R, TSH-R, PCNA, p53, PTH-R, MDR-1, MRP
Unkown Primary site	p53, Her2/neu, MDR-1, PCNA, CD31, CA-125	p53, Her2/neu, MDR-1, PCNA, CD31, CA-125, CD34, Ki-67, MPR, LRP, CEA (*) (**) (ξ) (ψ)

The use of various symbols in the comprehensive profiles is intended to provide the clinician with recommendations regarding additional panels that should be run in conjunction with the comprehensive profiles. These symbols represent various panels listed below in
5 Table 9. The symbols are defined as follows:

(ψ) – Cytogenic panel recommended

(χ) – Carcinoma of Unknown Primary Site panel recommended

(*f*) – Carcinoma panel recommended

(λ) – Epithelial panel recommended

10 (π) – Bladder vs. Prostate Carcinoma panel recommended

(♥) – Pituitary panel recommended

(∞) – Neuronal panel recommended

(*) – Growth Factor panel recommended

(ξ) – WBC Infiltration panel recommended

15 (**) – Oncogene/TSG panel recommended

TABLE 9

PANEL	BMMs
Angiogenesis Panel/Index-1	CD31, CD34, VEGFR, TSP-1, PDGFR-α chain
Angiogenesis Panel/Index-2	p53, TSP-1, CD31, [Indication for "at risk" occult metastasis]
Apoptosis Panel	P53, mdm-2, annexin, bcl-2, bax
Carcinoma of Unknown Primary Site Panel	PCNA, p53, Her-2, MDR, ER/PR/AR
Carcinoma of Unknown Primary Site with Metastasis to Spine or Bones Panel	Her-2, LRP, MDR, CEA, CA125, CD43 (males = PSMA)
Carcinoma vs. Lymphoma Panel	LCA, c-kit/myeloid marker = CD117, Ki-67
Epithelial Panel	Ber-EP4, B72.3, EGFR, EMA
Growth Factor-Receptor Panel	c-erb-2, EGFR, c-erb-1, VEGFR, PDGFR, TGFR –I&II [amplified –indication growth regulation & uncontrolled cell proliferation]
Heat Shock Protein Panel	HSP-PC96, HSP 70, HSP 90
Hormone Receptor Panel	ER/PR/AR
Invasion/Metastasis Panel	ICAM, uPa, Pai-2, Bcl-x, TM
Keratin Panel #1	Keratins #39, 43, 50
Keratin Panel #2	Keratins #45, 56
Keratin Panel #3	Keratins #34, 39, 40, 43, 48, 50, 50.6
Keratin Panel #4	Keratins #39, 40, 43, 48, 50, 50.6
Keratin Panel #5	Keratins #40-68
Lymph Node & Bone Marrow MicroMetastasis Panel	LK/AE-1, CD31, CD34
Lymphoma vs. Carcinoma Panel	LCA, c-kit/myeloid marker = CD117, Ki-67
Multidrug Resistance Panel #1	MDR-1, MPR, MGMT
Multidrug Resistance Panel	TS, LRP, Topoisomerase I&II

#2	
Neural Panel	CD56, GFAP, Leu7, MBP, NF, NSE, β2-Microglobulin, Syn, NSE, Ubiguitin
Neuroendocrine Panel	PGP 9.5, NSE, Chromogranin A, CEA
Neuroendocrine Gastrin Panel	Bombesin, CA19.9, CD56, Leu7
Occult Metastasis Panel #1	ICAM, uPA, Pai-2, Bcl-x, TM
Occult Metastasis Panel #2	p53, TSP-1, CD31
Oncogene/Tumor Suppressor Gene Panel #1	TNFR, TGFR, c-myc, p53, ras
Oncogene/Tumor Suppressor Gene Panel #2	c-fos, c-jun, c-myc, ras
Pituitary Panel	GH, IGF-I, TSH, Adrenocorticotropin, Prolactin
Proliferative Panel/Index	Ki-67, c-erb-2, PCNA
T & B Lymphocytes Panel	CD3, CD19/Leu12, CD45RO/A6, Leu17 (T-cells, B-cells, [Helper, Inducer T-cells], Activated T&B cells)
Unconventional Multidrug Resistance Panel	p53, bcl-2
Undifferentiated Carcinoma Panel	p53, Rb, APC, MCC, simple epithelial cytokeratins and squamous epithelial cytokeratins
Undifferentiated Tumor Panel	Calretinin, mucicarmine, CEA, B72.3
White Blood Cell Count Infiltration Panel #1	MCG, CD3, CD19/Leu-12, CD41/GPIIB/IIIA, CD45 (Macrophages, T-cells, B-cells, [platelets, megakaryocytes, megakaryoblasts], leukocytes)
White Blood Cell Count Infiltration Panel #2	MCG, CD3/Leu3a&b, CD45, CD14/MO2 (Magrophages, Helper T-cells, [Mature monocytes, granulocytes], Leukocytes)
White Blood Cell Count Infiltration Panel # 3	T&B cells = CD3, CD19/Leu12, CD45RO/A6, Leu17 (T-cells, B-cells, [Helper, Inducer T-cells], Activated T&B cells)

<u>Interpretation of Assay Results</u>

The final interpretation of the results of the foregoing basic and comprehensive profiles relative to a specific patient with a particular stage of tumor growth and treatment history will be left to the primary oncologist treating the patient. Positive results are

indicated by the presence of Class I BMMs above or below basal levels or the detection of any amount of Class II BMMs. Typically, the quantity of up-regulated or down-regulated Class I BMMs and detected Class II BMMs will be the primary interpretative indicators, together with their type.

5 1. One Class I BMM present at non-basal levels:

In this case, the assay evaluation results may be due to some non-cancer related health issue, such as pregnancy, normal menses, etc. Thus, a patient medical history evaluation is made to identify such issues. If there is no non-cancer related explanation for the assay result, the patient is designated as being possibly precancerous and the Class II BMM results 10 are consulted for cancer process information.

2. Two or more Class I BMMs present at non-basal levels:

If the profile demonstrates positive results for two Class I BMMs or Class II BMMs, there is usually a high risk or entering into an oncogenic state. The patient will be designated as precancerous and intervention, be it chemotherapy and/or radiation, may be necessary to 15 prevent the overt onset of cancer. If the profile demonstrates positive results for three or more Class I BMMs or Class II BMMs, the patient is designated a cancerous. First line chemotherapy and/or radiotherapy is performed. The results of the profile will dictate exactly what chemoregimen/radioregimen to follow based on BMM expression and concentration. In particular, a chemoregimen can be based on selecting a suite of BMM modulating drugs, such 20 as those described above, that are designed to target cells expressing nonbasal levels of Class I BMMs. The drugs will cap the Class I BMMs in such cells. A radioregimen can be based on tumor size and type as determined by the Class II BMMs.

Once a precancerous or cancerous patient has been treated, evaluation of BMM profiles will continue to be monitored to determine if treatment modalities have been 25 efficacious by up-regulation and down-regulation of the BMMs that were initially detected. Additional and possibly modified treatments may then follow.

Accordingly, a cancer comprehensive method for evaluating cancer protein patterns is described herein. Unlike conventional cancer diagnosis, the inventive method is not based on staging. It does not matter what stage the patient's tumor is in or what type it is. It also does 30 not matter whether cellular components or serum/plasma fluid are evaluated. An overt objective of the method is that in the future, stage 2, stage 3 or stage 4 treatment may become a thing of the past because tumors will be neutralized fast enough and early enough, thereby preventing growth progression. A further advantage of the disclosed method is that a

clinician can homogenate the tumor, liquefy it, reduce its size, and dilute it out. Large tumor segments are not required. A tumor can be evaluated in totality.

While various embodiments of the invention have been shown and described, it should be apparent that many variations and alternative embodiments could be implemented in accordance with the invention. It is understood, therefore, that the invention is not to be in any way limited except in accordance with the spirit of the appended claims and their equivalents.

CLAIMS

I Claim:

1 1. A method for characterizing a cancer tumor for medical diagnosis and treatment,
2 comprising:
3 determining a cancer protein pattern based on detected nonbasal levels of
4 biomolecular markers (BMMs) associated with a patient's tumor; and
5 selecting a cancer therapy regimen based on said cancer protein pattern for eradicating
6 the tumor.

1 2. A method in accordance with Claim 1 wherein said cancer therapy regimen is a first
2 line therapy.

1 3. A method in accordance with Claim 1 wherein said cancer therapy regimen is
2 customized to target cells that express BMMs in said cancer protein pattern above or below
3 basal levels.

1 4. A method in accordance with Claim 1 wherein said BMMs include proteins that can
2 be modulated by protein modulating drugs and said cancer therapy regimen includes protein
3 modulating drugs corresponding to one or more of said BMMs.

1 5. A method in accordance with Claim 4 wherein said protein modulating drugs are
2 selectively combined into a chemo-suite that directly corresponds to said BMM pattern.

1 6. A method in accordance with Claim 1 wherein said BMMs include Class I BMMs
2 representing either tumor promoting or tumor suppressor proteins and Class II BMMs
3 representing tumor marker proteins that provide information about cancer progression.

1 7. A method in accordance with Claim 6 wherein said cancer therapy regimen is selected
2 by evaluating said Class I BMMs for upregulation or downregulation and evaluating said
3 Class II BMMs if any of said Class I BMMs are upregulated or downregulated.

1 8. A method in accordance with Claim 7 wherein said cancer therapy regimen is selected
2 by evaluating said Class I BMMs to determine if only one Class I BMM is upregulated or
3 downregulated, and if so, designating the patient as being possibly precancerous.

1 9. A method in accordance with Claim 7 wherein said cancer therapy regimen is selected
2 by evaluating said Class I BMMs to determine if only two Class I BMMs are upregulated or
3 downregulated, and if so, designating the patient as being precancerous.

1 10. A method in accordance with Claim 7 wherein said cancer therapy regimen is selected
2 by evaluating said Class I BMMs to determine if three or more Class I BMMs are
3 upregulated or downregulated, and if so, designating the patient as being cancerous.

1 11. A method for medical diagnosis and treatment of cancer, comprising:
2 obtaining an assay evaluation sample from a patient;
3 simultaneously testing said assay evaluation sample for upregulated or downregulated
4 biomolecular markers (BMMs) representing a cancer protein pattern; and
5 selecting a cancer therapy regimen based on said cancer protein pattern.

1 12. A method in accordance with Claim 11 wherein said assay evaluation sample
2 comprises a homogenate of a solid tumor sample obtained from the patient.

1 13. A method in accordance with Claim 11 wherein said assay evaluation sample
2 comprises a blood serum/plasma sample obtained from the patient.

1 14. A method in accordance with Claim 11 wherein said testing step is completed within
2 24-48 hours of obtaining said assay evaluation sample.

1 15. A method in accordance with Claim 11 wherein said cancer therapy regimen is a first
2 line cancer therapy regimen.

1 16. A method in accordance with Claim 11 wherein said cancer therapy regimen is a first
2 line radiotherapy regimen.

1 17. A method in accordance with Claim 11 wherein said cancer therapy regimen is a
2 chemotherapy regimen using a suite of chemotherapy agents directly corresponding to said
3 cancer protein pattern.

1 18. A method in accordance with Claim 17 wherein said chemotherapy agents are protein
2 modulating drugs that each respectively modulate one BMM of said cancer protein pattern.

1 19. A method in accordance with Claim 11 wherein said testing step includes
2 simultaneously testing said assay evaluation sample for Class I BMMs representing either
3 tumor promoting or tumor suppressor proteins and Class II BMMs representing tumor marker
4 proteins that provide information about cancer progression.

1 20. A method for characterizing a cancer tumor for medical diagnosis and treatment,
2 comprising:
3 obtaining an assay evaluation sample from a patient, said assay evaluation sample
4 being either a homogenate of a solid tumor sample obtained from the patient or a blood
5 serum/plasma sample obtained from the patient;
6 determining a cancer protein pattern based on detected nonbasal levels of
7 biomolecular markers (BMMs) associated with the patient's tumor;
8 selecting a cancer therapy regimen based on said cancer protein pattern for eradicating
9 the tumor;
10 said cancer therapy regimen being a first line therapy regimen customized to target
11 cells that express BMMs in said cancer protein pattern above or below basal levels;
12 said BMMs including proteins that can be modulated by protein modulating drugs and
13 said cancer therapy regimen including protein modulating drugs corresponding to one or
14 more of said BMMs;
15 said protein modulating drugs being selectively combined into a chemo-suite that
16 directly corresponds to said BMM pattern;
17 said BMMs including Class I BMMs representing either tumor promoting or tumor
18 suppressor proteins and Class II BMMs representing tumor marker proteins that provide
19 information about cancer progression;
20 said cancer therapy regimen being selected by evaluating said Class I BMMs for
21 upregulation or downregulation and evaluating said Class II BMMs if any of said Class I
22 BMMs are upregulated or downregulated;
23 said cancer therapy regimen being selected by evaluating said Class I BMMs to
24 determine if only one Class I BMM is upregulated or downregulated, and if so, designating
25 the patient as being possibly precancerous;
26 said cancer therapy regimen being further selected by evaluating said Class I BMMs

27 to determine if only two Class I BMMs are upregulated or downregulated, and if so,
28 designating the patient as being precancerous; and
29 said cancer therapy regimen being further selected by evaluating said Class I BMMs
30 to determine if three or more Class I BMMs are upregulated or downregulated, and if so,
31 designating the patient as being cancerous.

1 21. A method for characterizing a cancer tumor for medical diagnosis and treatment,
2 comprising:
3 determining a cancer protein pattern based on detected nonbasal levels of
4 biomolecular markers (BMMs) associated with a patient's tumor;
5 selecting a cancer therapy regimen based on said cancer protein pattern for eradicating
6 the tumor; and
7 said method being specific to one or more particular cancer types and implemented as
8 either a basic profile comprising a first set of BMMs or a comprehensive profile comprising
9 said first set of BMMs and a second set of BMMs.

1 22. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic ovarian profile with said first set of BMMs comprising ER/PR, Her2/neu, MRP, LRP
3 and EGFR.

1 23. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive ovarian profile with said first and second sets of BMMs comprising
3 ER/PR/AR, Her2/neu, MRP, LRP, EGFR, CA-125, CU-18, PCNA, DF 3, uPA.

1 24. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic ovarian/peritoneal profile with said first set of BMMs comprising S-100, PCNA, MDR-
3 1, EGFR, ER/PR/AR.

1 25. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive ovarian/peritoneal profile with said first and second sets of BMMs
3 comprising S-100, PCNA, MDR-1, EGFR, ER/PR/AR, Ki-67, p53, Her2/neu, MRP, LRP,
4 EGFR, CA-125, uPA.

1 26. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic ovarian/gall bladder/peritoneal profile with said first set of BMMs comprising S-100,
3 PCNA, MDR-1, EGFR ER/PR/AR, PP, p53, c-myc.

1 27. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive ovarian/gall bladder/peritoneal profile with said first and second sets of
3 BMMs comprising S-100, PCNA, MDR-1, EGFR ER/PR/AR, PP, MRP, S-100, NSE, LMW
4 Keratin, p53, TS, CD43, CEA, CD31, CA 242, c-myc, PDECGF, VIP.

1 28. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic ademo-carcinoma profile with said first set of BMMs comprising ACTH, B72.3,
3 BCA225, Bcl-2, CA15.3.

1 29. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive ademo-carcinoma profile with said first and second sets of BMMs comprising
3 ACTH, B72.3, BCA225, Bcl-2, CA15.3, CA125, CEA/D-14, CyclinD1, PCNA, Ki-67, MRP,
4 MDR-1.

1 30. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic bladder profile with said first set of BMMs comprising p53, Her2/neu (p185), PCNA,
3 MDR-1, EGFR.

1 31. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive bladder profile with said first and second sets of BMMs comprising p53,
3 Her2/neu (p185), PCNA, MDR-1, EGFR, Ki-67, pan-ras, Bcl-2, Bcl-x, Rb.

1 32. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic brain profile with said first set of BMMs comprising p53, Her2/neu, MGMT, Ki-67,
3 MDR-1, GFAP, Syn.

1 33. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive brain profile with said first and second sets of BMMs comprising p53,
3 Her2/neu, MGMT, Ki-67, MDR-1, GFAP, Syn, CD35, CD31, PCNA, VEGFR, PDGFR.

1 34. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic breast profile with said first set of BMMs comprising ER/PR, Her2/neu, TS, BCA-125,
3 MDR-1, MRP.

1 35. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive breast profile with said first and second sets of BMMs comprising ER/PR,
3 Her2/neu, TS, BCA-125, MDR-1, MRP, CA-125, p53, CD31, CA 125, DF 3, VEGFR.

1 36. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic colon/bowel profile with said first set of BMMs comprising p53, TS, CD43, CEA,
3 PCNA.

1 37. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive colon/bowel profile with said first and second sets of BMMs comprising p53,
3 TS, CD43, CEA, PCNA, MDR-1, CD31, CA 242, c-myc, PDECGF, VIP.

1 38. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic endometrial profile with said first set of BMMs comprising ER/PR, Ki-67, p53, MDR-
3 1.

1 39. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive endometrial profile with said first and second sets of BMMs comprising
3 ER/PR, Ki-67, p53, MDR-1, CD31, CA-125, MPR, TSP, ras.

1 40. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic lung profile with said first set of BMMs comprising p53, LRP, NSE, MDR-1 CEA, CA-
3 125.

1 41. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive lung profile with said first and second sets of BMMs comprising p53, LRP,
3 NSE, MDR-1 CEA, CA-125, bcl-2, Cyfra 21-1, CA 19-9, MGMT, MRP.

1 42. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic melanoma profile with said first set of BMMs comprising MDR-1, p53, CD31, HMB-
3 45, MRP, EGFR, Involucrin.

1 43. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive melanoma profile with said first and second sets of BMMs comprising MDR-
3 1, p53, CD31, HMB-45, MRP, EGFR, Involucrin, Bcl-2, c-myc, PCNA, Ki67, NIKI.

1 44. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic oral profile with said first set of BMMs comprising p53, MDR-1, MRP, EGFR, PCNA,
3 CA-125.

1 45. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive oral profile with said first and second sets of BMMs comprising p53, MDR-1,
3 MRP, EGFR, PCNA, CA-125.

1 46. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic peritoneal profile with said first set of BMMs comprising CA19.9, Gastrin, S-100,
3 PCNA, NSE.

1 47. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive peritoneal profile with said first and second sets of BMMs comprising
3 CA19.9, Gastrin, S-100, PCNA, NSE, MDR, MRP, Ki-67, p53, EGFR.

1 48. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic prostrate profile with said first set of BMMs comprising AR, HPAP, PSMA, c-erb-2,
3 Ki-67, GRP.

1 49. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive prostrate profile with said first and second sets of BMMs comprising AR,
3 HPAP, PSMA, c-erb-2, Ki-67, GRP, p53, MDR-1, P-cadherin, VEGF, CD31.

1 50. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic sarcoma profile with said first set of BMMs comprising p53, MDR-1, MRP, EGFR,
3 O13.

1 51. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive sarcoma profile with said first and second sets of BMMs comprising p53,
3 MDR-1, MRP, EGFR, O13, VEGR, Bcl-2, c-myc, PCNA, Ki-67.

1 52. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic stomach profile with said first set of BMMs comprising CA19.9, Gastrin, PP, PCNA,
3 MDR-1, S-100, HBP-P.

1 53. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive stomach profile with said first and second sets of BMMs comprising CA19.9,
3 Gastrin, PP, PCNA, MDR-1, S-100, HBP-P, NSE, LMW Keratin, Villin.

1 54. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic thyroid profile with said first set of BMMs comprising Iodine-R, Thyro-R, TSH-R,
3 PCNA, p53.

1 55. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive thyroid profile with said first and second sets of BMMs comprising Iodine-R,
3 Thyro-R, TSH-R, PCNA, p53, PTH-R, MDR-1, MRP.

1 56. A method in accordance with Claim 21 wherein said method is implemented as a
2 basic unknown primary site profile with said first set of BMMs comprising p53, Her2/neu,
3 MDR-1, PCNA, CD31, CA-125.

1 57. A method in accordance with Claim 21 wherein said method is implemented as a
2 comprehensive unknown primary site profile with said first and second sets of BMMs
3 comprising p53, Her2/neu, MDR-1, PCNA, CD31, CA-125, CD34, Ki-67, MPR, LRP, CEA.

1 58. A method for characterizing a cancer tumor for medical diagnosis and treatment,
2 comprising:

3 determining a cancer protein pattern based on detected nonbasal levels of
4 biomolecular markers (BMMs) associated with a patient's tumor;
5 selecting a cancer therapy regimen based on said cancer protein pattern for eradicating
6 the tumor; and
7 said method being implemented as a panel comprising a set of BMMs selected to
8 provide cancer diagnostic information.

1 59. A method in accordance with Claim 58 wherein said method is implemented as an
2 angiogenesis panel with said BMMs comprising CD31, CD34, VEGFR, TSP-1, PDGFR-α
3 chain.

1 60. A method in accordance with Claim 58 wherein said method is implemented as an
2 angiogenesis panel with said BMMs comprising p53, TSP-1, CD31.

1 61. A method in accordance with Claim 58 wherein said method is implemented as an
2 apoptosis panel with said BMMs comprising P53, mdm-2, annexin, bcl-2, bax.

1 62. A method in accordance with Claim 58 wherein said method is implemented as an
2 apoptosis panel with said BMMs comprising P53, mdm-2, annexin, bcl-2, bax.

1 63. A method in accordance with Claim 58 wherein said method is implemented as a
2 carcinoma of unknown site panel with said BMMs comprising PCNA, p53, Her-2, MDR,
3 ER/PR/AR.

1 64. A method in accordance with Claim 58 wherein said method is implemented as a
2 carcinoma of unknown site with metastasis to spine or bones panel with said BMMs
3 comprising Her-2, LRP, MDR, CEA, CA125, CD43, PSMA.

1 65. A method in accordance with Claim 58 wherein said method is implemented as a
2 carcinoma vs. Lymphoma panel with said BMMs comprising LCA, c-kit/myeloid marker =
3 CD117, Ki-67.

1 66. A method in accordance with Claim 58 wherein said method is implemented as an
2 epithelial panel with said BMMs comprising Ber-EP4, B72.3, EGFR, EMA.

1 67. A method in accordance with Claim 58 wherein said method is implemented as a
2 growth factor receptor panel with said BMMs comprising c-erb-2, EGFR, c-erb-1, VEGFR,
3 PDGFR, TGFR–I&II.

1 68. A method in accordance with Claim 58 wherein said method is implemented as a heat
2 shock protein panel with said BMMs comprising HSP-PC96, HSP 70, HSP 90.

1 69. A method in accordance with Claim 58 wherein said method is implemented as a
2 hormone receptor panel with said BMMs comprising ER/PR/AR.

1 70. A method in accordance with Claim 58 wherein said method is implemented as an
2 invasion metastasis panel with said BMMs comprising ICAM, uPa, Pai-2, Bcl-x, TM.

1 71. A method in accordance with Claim 58 wherein said method is implemented as a
2 keratin panel with said BMMs comprising Keratins #39, 43, 50.

1 72. A method in accordance with Claim 58 wherein said method is implemented as a
2 keratin panel with said BMMs comprising Keratins #45, 56.

1 73. A method in accordance with Claim 58 wherein said method is implemented as a
2 keratin panel with said BMMs comprising Keratins #34, 39, 40, 43, 48, 50, 50.6.

1 74. A method in accordance with Claim 58 wherein said method is implemented as a
2 keratin panel with said BMMs comprising Keratins #40-68.

1 75. A method in accordance with Claim 58 wherein said method is implemented as a
2 lymph node and bone marrow micrometastasis panel with said BMMs comprising LK/AE-1,
3 CD31, CD34.

1 76. A method in accordance with Claim 58 wherein said method is implemented as a
2 lymphoma versus carcinoma panel with said BMMs comprising LCA, c-kit/myeloid marker
3 = CD117, Ki-67.

1 77. A method in accordance with Claim 58 wherein said method is implemented as a
2 multidrug resistance panel with said BMMs comprising MDR-1, MPR, MGMT.

1 78. A method in accordance with Claim 58 wherein said method is implemented as a
2 multidrug resistance panel with said BMMs comprising TS, LRP, Topoisomerase I&II.

1 79. A method in accordance with Claim 58 wherein said method is implemented as a
2 neural panel with said BMMs comprising CD56, GFAP, Leu7, MBP, NF, NSE, β2-
3 Microglobulin, Syn, NSE, Ubiguitin.

1 80. A method in accordance with Claim 58 wherein said method is implemented as a
2 neuroendocrine panel with said BMMs comprising PGP 9.5, NSE, Chromogranin A, CEA.

1 81. A method in accordance with Claim 58 wherein said method is implemented as a
2 neuroendocrine gastrin panel with said BMMs comprising Bombesin, CA19.9, CD56, Leu7.

1 82. A method in accordance with Claim 58 wherein said method is implemented as an
2 occult metastasis panel with said BMMs comprising ICAM, uPA, Pai-2, Bcl-x, TM.

1 83. A method in accordance with Claim 58 wherein said method is implemented as an
2 occult metastasis panel with said BMMs comprising p53, TSP-1, CD31.

1 84. A method in accordance with Claim 58 wherein said method is implemented as an
2 oncogene/tumor suppressor gene panel with said BMMs comprising TNFR, TGFR, c-myc,
3 p53, ras.

1 85. A method in accordance with Claim 58 wherein said method is implemented as an
2 oncogenene/tumor suppressor gene panel with said BMMs comprising c-fos, c-jun, c-myc,
3 ras.

1 86. A method in accordance with Claim 58 wherein said method is implemented as a
2 pituitary panel with said BMMs comprising GH, IGF-I, TSH, Adrenocorticotropin, Prolactin.

1 87. A method in accordance with Claim 58 wherein said method is implemented as a
2 proliferative panel with said BMMs comprising Ki-67, c-erb-2, PCNA.

1 88. A method in accordance with Claim 58 wherein said method is implemented as an T
2 & B lymphocytes panel with said BMMs comprising CD3, CD19/Leu12, CD45RO/A6,
3 Leu17 (T-cells, B-cells, [Helper, Inducer T-cells], Activated T&B cells).

1 89. A method in accordance with Claim 58 wherein said method is implemented as an
2 unconventional multidrug resistance panel with said BMMs comprising p53, bcl-2.

1 90. A method in accordance with Claim 58 wherein said method is implemented as an
2 undifferentiated carcinoma panel with said BMMs comprising p53, Rb, APC, MCC, simple
3 epithelial cytokeratins and squamous epithelial cytokeratins.

1 91. A method in accordance with Claim 58 wherein said method is implemented as an
2 undifferentiated tumor panel with said BMMs comprising calretinin, mucicarmine, CEA,
3 B72.3.

1 92. A method in accordance with Claim 58 wherein said method is implemented as a
2 white blood cell count panel with said BMMs comprising MCG, CD3, CD19/Leu-12,
3 CD41/GPIIB/IIIA, CD45 (Macrophages, T-cells, B-cells, [platelets, megakaryocytes,
4 megakaryoblasts], leukocytes).

1 93. A method in accordance with Claim 58 wherein said method is implemented as a
2 white blood cell count panel with said BMMs comprising MCG, CD3/Leu3a&b, CD45,
3 CD14/MO2 (Magrophages, Helper T-cells, [Mature monocytes, granulocytes], Leukocytes).

1 94. A method in accordance with Claim 58 wherein said method is implemented as a
2 white blood cell count panel with said BMMs comprising T&B cells = CD3, CD19/Leu12,
3 CD45RO/A6, Leu17 (T-cells, B-cells, [Helper, Inducer T-cells], Activated T&B cells).

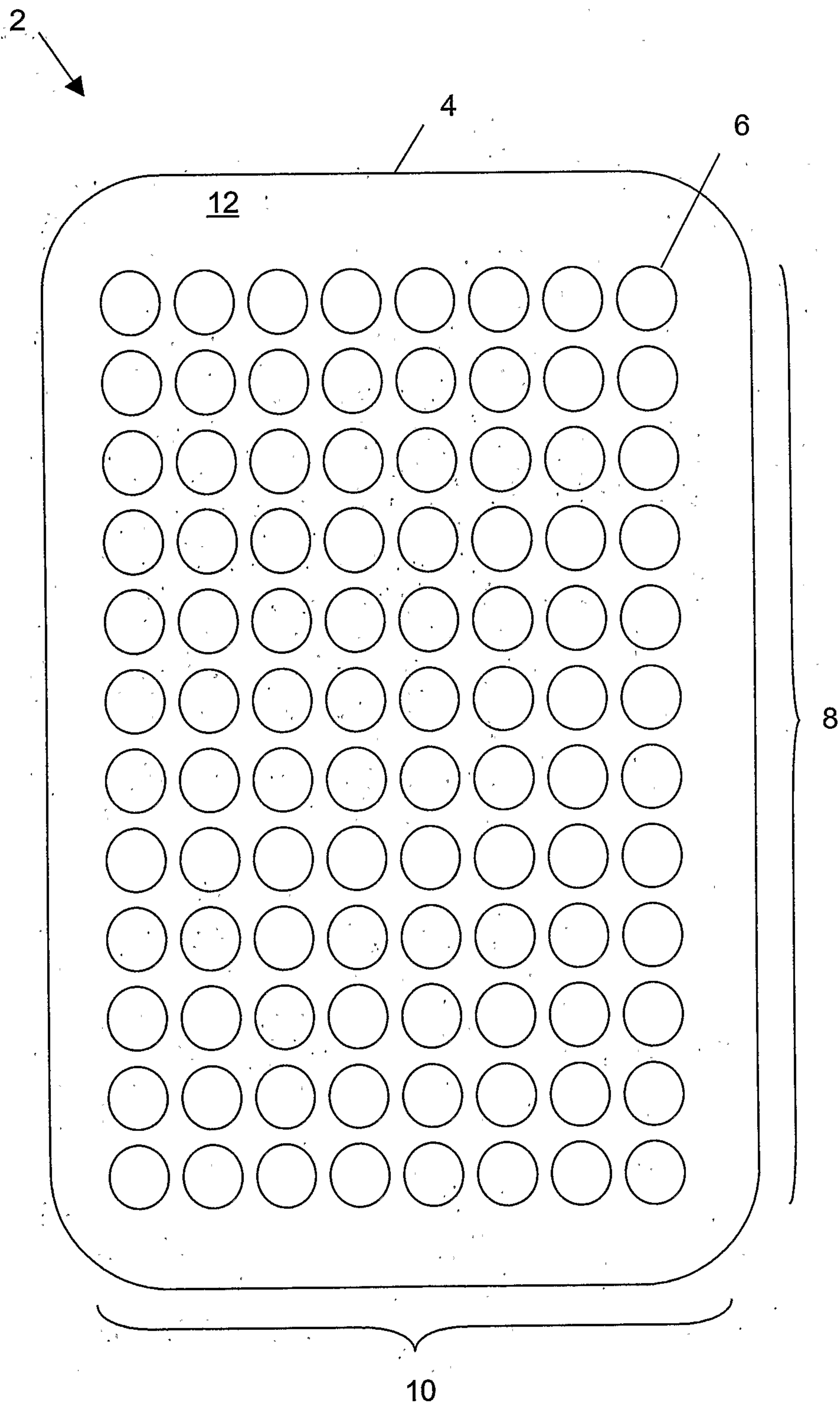

FIG. 1

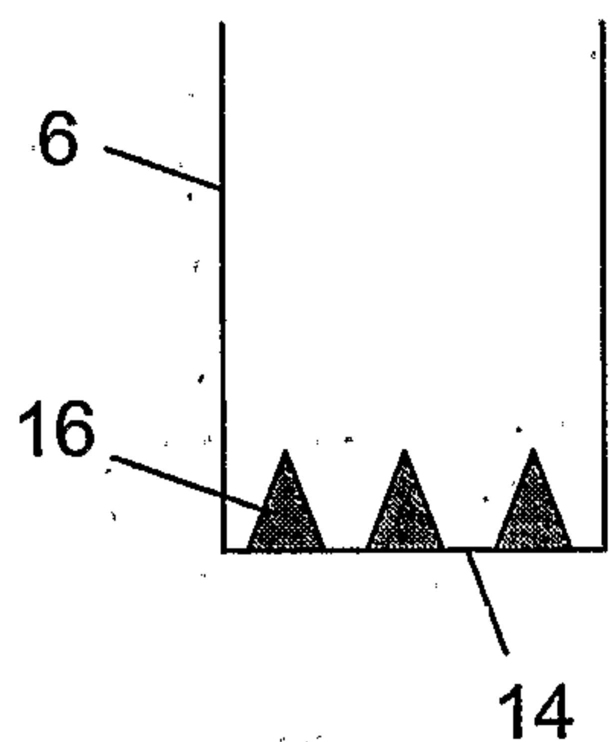

FIG. 2A

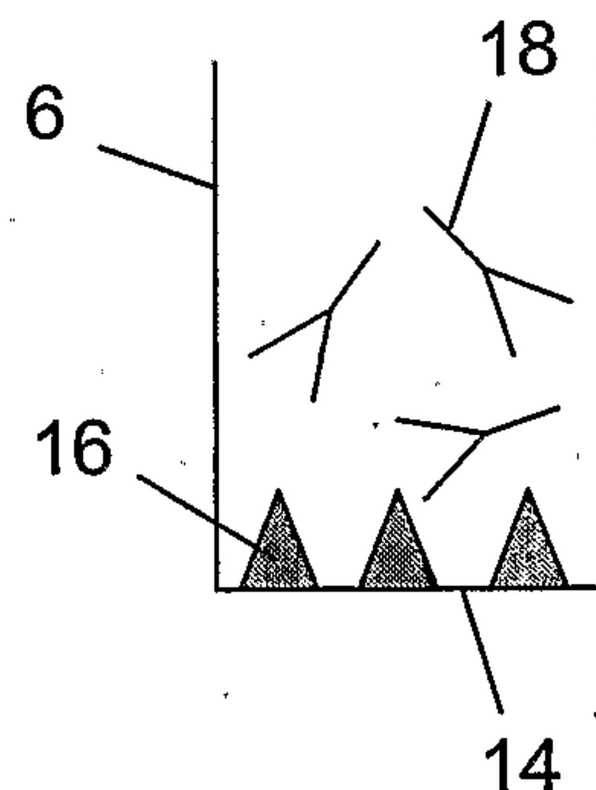

FIG. 2B

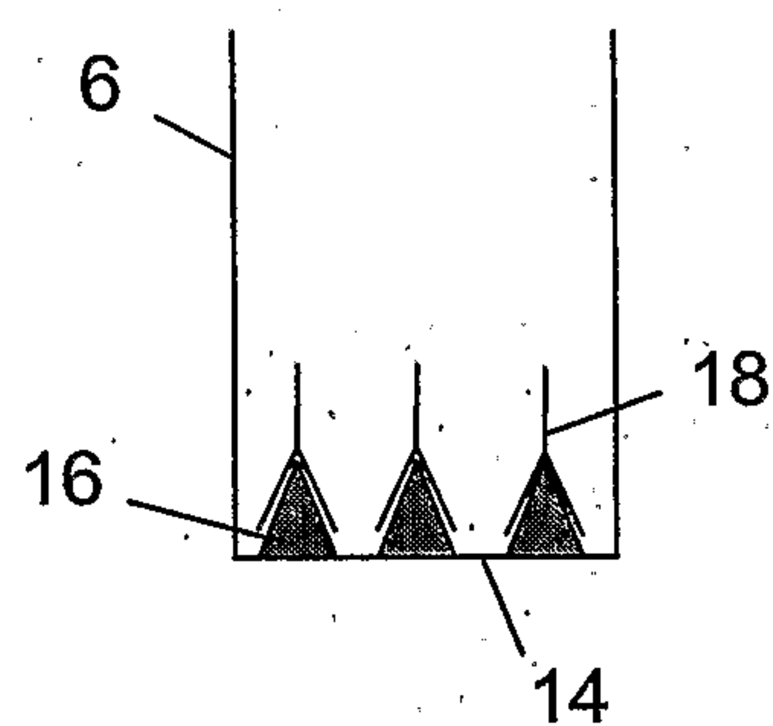

FIG. 2C

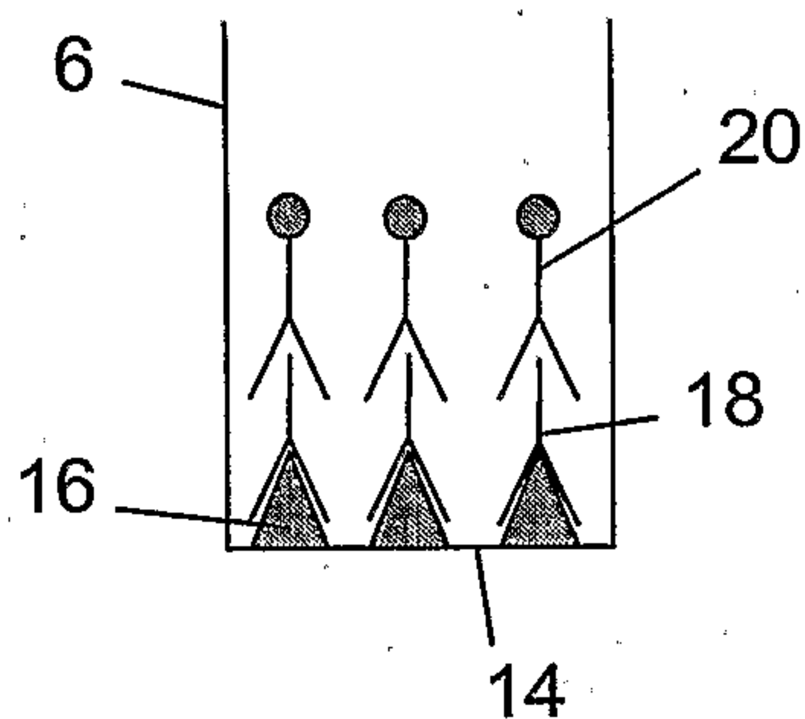

FIG. 2D

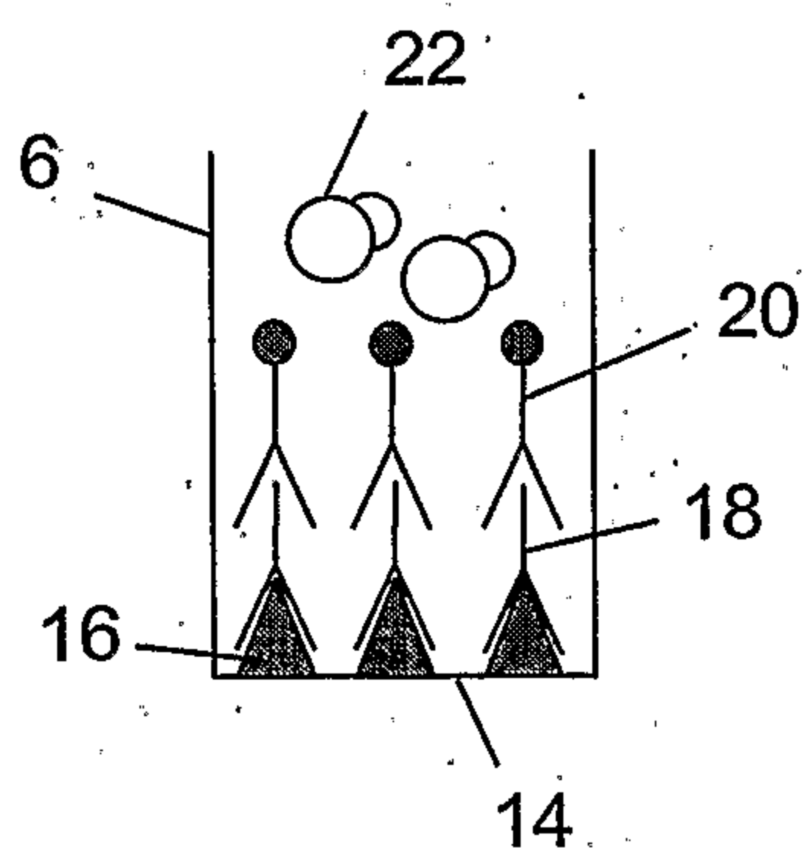

FIG. 2E

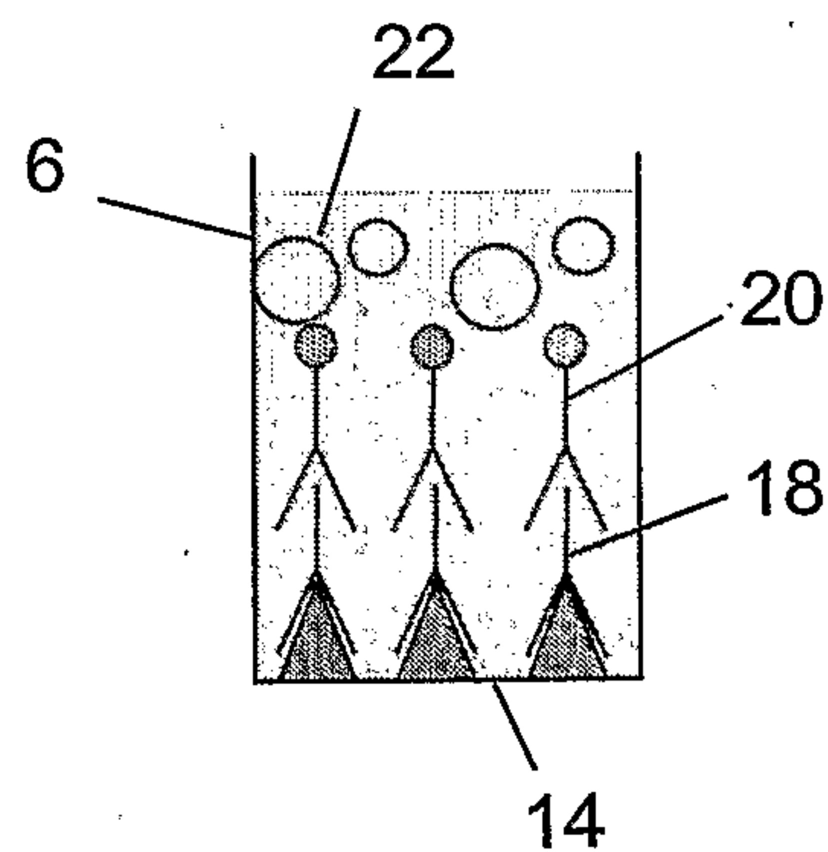

FIG. 2F

	#1	#2	#3	#4	#5	#6	#7	#8
#1	X							
#2								
#3								
#4								
#5								
#6								
#7								
#8								
#9								
#10	PT.	PT.	PT.	PT.	PT.	PT.	PT.	PT.
#11	PT.	PT.	PT.	PT.	PT.	PT.	PT.	PT.
#12	PT.	PT.	PT.	PT.	PT.	PT.	PT.	PT.

FIG. 3

	#1	#2	#3	#4	#5	#6	#7	#8
#1	X							
#2								
#3								
#4								
#5								
#6								
#7								
#8								
#9								
#10	PT.	PT.	PT.	PT.	PT.	PT.	PT.	PT.
#11	PT.	PT.	PT.	PT.	PT.	PT.	PT.	PT.
#12	PT.	PT.	PT.	PT.	PT.	PT.	PT.	PT.