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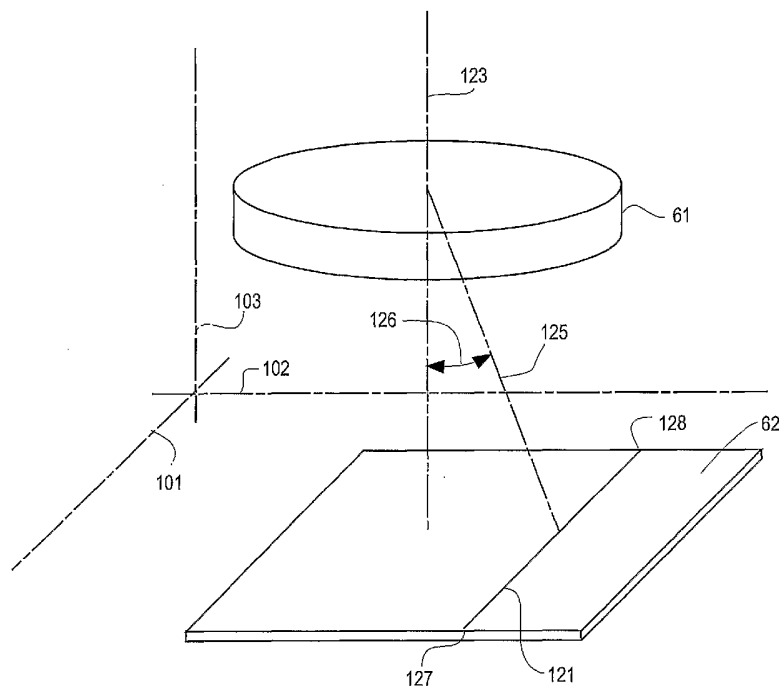
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(54) Title: LIGHT SCATTERING PRODUCT RANKS HIV/AIDS TREATMENTS



(57) Abstract: By comparing angular intensity distributions of light scattered by cells from the blood of a person infected with at least one of HIV/AIDS viruses with, and without, a treatment from a plurality of antiviral treatments added, the potency of treatments for that person can be ranked, where the comparison can comprise calculations of correlation coefficients.

Description

LIGHT SCATTERING PRODUCT RANKS HIV/AIDS TREATMENTS

- [1] This application claims benefit of U. S. provisional application 60/669,191 filed 06 April 2005, which is incorporated herein by reference.
- [2] The product uses light scattered by blood from a person infected with at least one variant of the human immunodeficiency virus with - and without - candidate treatments added in order to rank the potency of the candidate treatments specifically for the person.
- [3] FIG. 1 shows the ranking schematically.
- [4] FIG. 2 shows the light scattering schematically.
- [5] The product comprises a ranking signal **40** which ranks the potency of antiviral treatments from a treatment plurality of antiviral treatments. The ranking signal is caused by at least a control signal **13** and by at least a subset of a treatment signal plurality **30**. The ranking signal represents at least comparisons between at least some of the subset of the treatment signal plurality and the control signal. The subset necessarily has more than one member of the treatment signal plurality.
- [6] The control signal **13** represents at least a control measurement of a control scattered light intensity distribution. The control scattered light intensity distribution comprises control incident light scattered **14** by a control sample of cells **12**. The control sample **12** comprises a control plurality of sample cells from a sample **11** of cells. The sample of cells comprises cells from blood of a person infected with at least one variant of human immunodeficiency virus variants.
- [7] The treatment signal plurality **20** represents at least a plurality of treatment measurements of a treatment distribution plurality of treatment scattered light intensity distributions. The treatment distribution plurality **30** comprises treatment incident light scattered respectively from each *I*th member of a treatment sample plurality of treatment samples of cells. Each *I*th member of the treatment sample plurality comprises an *I*th treatment plurality of cells from the sample of cells with an *I*th treatment from a treatment plurality of antiviral treatments added.
- [8] The control incident light and the treatment incident light can be from two separate light sources, can be from the one light source, and can be from portions of one light source. The control measurement and the treatment measurements can be made by two, and more, separate imagers, can be one imager, and can be portions of one imager. The control scattered light intensity distribution and the treatment distribution plurality can be obtained in serial measurements, in one multi-component measurement, by beam splitting means, and in combinations of these. 'Imager' means any device which can measure light intensity.
- [9] The control signal and the treatment signal plurality must be comparable. This can

be achieved in various ways. For example, the conditions of the imagings can be interchangeable, except for the added treatment, so that the control signal and members of the treatment signal plurality light are directly comparable. For example, imagings can be calibrated with a standard imaging, so that the control signal and members of the treatment signal plurality are comparable via calibrations.

- [10] The control scattered light intensity distribution and the treatment distribution plurality are obtained using the light scattering taught in US patent application 10/416,099 filed 06 May 2003 published as US20040043433-A1 on 04 March 2004, which is incorporated herein by reference, and which is a 371 of PCT application PCT/US02/02132 filed 25 January 2002 and published as WO02/077748 03 October 2002, which claims priority of US provisional application 60/265,761 filed 01 February 2001.
- [11] The light scattering is shown schematically in FIG. 2. Relative to orthogonal axis triad **101**, **102**, **103**, a sensitive surface **62** of an imager is parallel to the **101**, **102** plane and orthogonal to the **103** axis. The central ray **123** of incident light is parallel to the **103** axis. A scattered ray of light **125** which is scattered by a control or treatment sample **61** is at an angle **126** from the central ray **123** and intersects the sensitive surface **62** at a line **121** which extends between edges **127** and **128** of the sensitive surface and which is parallel to the **101** axis.
- [12] For a given value of the scattering angle **126**, values of the scattered light intensity detected by the imager can be averaged along the **121** line and can be averaged for multiple exposures of the imager. This is repeated for multiple values of the scattering angle **126**. The result is the control scattered light intensity distribution for the control sample when **61** is the control sample. The result is the *I*th member of the treatment distribution plurality when **61** is the *I*th member of the treatment sample plurality.
- [13] Various imaging means have been used. Scattered light can illuminate a screen which can be imaged. Scattered light can be imaged directly. Incident light in the range 780 to 820 nanometers works well because this minimizes absorption and anomalous dispersion. The incident light wavelength can be tailored within this range and outside of this range to meet various needs. Off-the-shelf imagers sensitive in the near infrared work well. Imagers with more sophisticated read out capacity can be used in more automated versions of the product.
- [14] In the HIV/AIDS case the angular intensity distributions to an angle of about 5 degrees produce useful results. Useful results can also be obtained from distributions extending to larger angles. A beam stop can intercept the central portion of light to protect the imager so that about the first 0.5 degrees of the angular distribution is intercepted. Other instrumentation designs could reduce the amount of intercepted angular distribution in order to get better data.
- [15] The wave front of the scattered light is spherical. There are several ways this can be accommodated: the imaging surface can be spherical, the imaging data can be

corrected for a non-spherical imaging surface, and the thickness of all the samples along the central axis of the input light can be small enough so that it is not necessary to correct for the non-spherical shape of the imaging surface. For example, in one configuration of the input light source, the samples, and the imager, the correction is unnecessary at one millimeter sample thickness and necessary at five millimeters sample thickness.

- [16] The light scattering produces useful results if the sample is whole blood. Higher signal-to-noise ratios are obtained if the sample is mainly white cells. In the HIV/AIDS case even better results are obtained when the sample is mainly peripheral blood mononuclear cells.
- [17] Useful results are obtained when the treatments added to the sample to form members of the treatment plurality are in IC50 concentrations. In this case - and when the sample is mainly peripheral blood mononuclear cells - the incubation time for treatments is about 40 minutes at 37 degrees Celsius.
- [18] Treatment samples can have combinations of antivirals added to cells from the sample. Antivirals can be in gels so that treatment samples are formed by adding cells from the sample to the gels.
- [19] In order to rank treatments some measure is needed for a difference in scattered light intensity distributions between members of the treatment sample plurality and the control sample. There are many ways to do this.
- [20] One way to do this is to compare correlation coefficients pairing each member of the treatment signal plurality with the control signal. Also, correlation coefficients for each member of treatment signal plurality can be paired with each other member of the treatment signal plurality.
- [21] There are many ways to calculate these correlation coefficients. Calculation of Pearson's rank correlation coefficients and Spearman's rank correlation coefficients produce useful results.
- [22] Members of the array 40 shown in FIG. 1 can be Pearson's rank coefficients and can be Spearman's rank coefficients. The bottom CS row 41 shows the rank coefficients - RC1 through RCN - which are for the control signal CS paired in turn with each member of a treatment signal plurality TS1 through TSN. The lowest rank coefficient in this row indicates the member of the treatment plurality which is most potent for this particular sample of blood.
- [23] The TSN row - just above 41 - shows the rank coefficients for the TSN treatment signal paired with each of the other members of the treatment signal plurality. The TSI row 42 shows the rank coefficients for the Ith member of the treatment signal plurality paired with other members of the treatment signal plurality. (The array is symmetric about the diagonal with rank coefficients of 1.) The highest of the rank coefficients in all but the bottom CS row indicates the member of the treatment plurality which is most alike the most potent treatment and can be usefully combined with the most

potent.

- [24] In variations of this product the control sample can be from the sample with a control treatment added. The control sample can be from the sample with a plurality of control treatments added.
- [25] The control signal is caused by the control imager when the control imager detects the control scattered light intensity distribution. This can happen in multiple iterations. A component of the control signal from an iteration can be signal connected with an information system via a signal connection. The information system can use multiple components from the multiple iterations to cause the control signal. The information system can be remote from the control imager. The signal connection can be wired, wireless, and combinations of these.
- [26] The treatment signal plurality can be caused in the same manner. The ranking signal can be caused by the information system.
- [27] A 'signal' from a product part to a second product part - and a product part being 'signal connected' with a second product part - here, and throughout, mean that a physical state of the product part causes a second physical state of the second product part. This can occur by various direct causal means and can occur by any of various transmission means. Transmitted signals can be any of various point-to-point and broadcast forms of energy transmission such as wireless and via wires, cables, and fibers. Parts of transmitted signals can reside with one form of the transmitted signal, parts can reside with a second form of transmitted signal, and parts can reside with various combinations of transmitted signals.
- [28] Direct causal means and transmission means can be any means by which a first physical state can produce a second physical state. For example, these can be - but are not limited to - mechanical means, pneumatic means, acoustic means, electromagnetic means, entanglement means, and combinations of two and more of these.
- [29] The several causes here can act via any of various processing modes. The processing can utilize configured processing elements such as fixed circuits, can utilize configurable processing elements such as field programmable gate arrays and neural networks, can utilize instructions in a signal-bearing medium, and can utilize combinations of these. The processing can be by stand alone means, can act via a local information system, can act via a networked information system, and can act via combinations of these. The processing - in part at least - can be by parts of an imager. The signal-bearing medium can be a transmitted signal, a storage medium, and a combination of a transmitted signal and a storage medium.
- [30] The light scattering product ranking HIV/AIDS treatments comprises a device which produces the ranking signal and comprises the method by which the device produces the ranking signal.
- [31] The product can use any means to prepare the control sample and the treatment sample plurality, to cause the control signal and the treatment signal plurality by light

scattering, and to use the control signal and the treatment signal plurality to cause the ranking which cause functionally equivalent results.

Claims

[1]

Claimed is:

1. A light scattering product for ranking human immunodeficiency virus treatments, the product comprising:
a control signal representing at least a control measurement of a control scattered light intensity distribution,
the control scattered light intensity distribution comprising control incident light scattered by a control sample of cells.
the control sample of cells comprising a control plurality of cells from a sample of cells,
the sample of cells comprising cells from blood of a person infected with at least one variant from a viral plurality of human immunodeficiency virus variants;
a treatment signal plurality representing at least a plurality of treatment measurements of a treatment distribution plurality of treatment scattered light intensity distributions,
the treatment distribution plurality comprising treatment incident light scattered respectively from each Ith member of a treatment sample plurality of treatment samples of cells,
each Ith member of the treatment sample plurality comprising an Ith treatment plurality of cells from the sample of cells with an Ith treatment from a treatment plurality of antiviral treatments added;
a ranking signal which is caused by at least the control signal and by at least a subset of the treatment signal plurality,
the ranking signal representing at least comparisons between at least some of the subset of the treatment signal plurality and the control signal.
2. The product of claim 1 wherein the ranking signal represents at least correlation coefficients between at least some of the subset of the treatment signal plurality paired with the control signal.
3. The product of claim 2 wherein the ranking signal also represents comparisons between at least some of the subset of the treatment signal plurality and other members of the treatment signal plurality.
4. The product of claim 2 wherein the ranking signal also represents correlation coefficients of at least some of the subset of the treatment signal plurality paired with other members of the treatment signal plurality.
5. The product of claim 1 wherein effects of a scattered light wavefront curvature are minimized by an imager curvature.
6. The product of claim 1 wherein effects of a scattered light wavefront curvature are minimized by mathematical correction.
7. The product of claim 1 wherein effects of a scattered light wavefront curvature are minimized by imager configurations relative to scatterers.

8. A light scattering method for ranking human immunodeficiency virus treatments, the method comprising the steps of:
causing a control signal representing at least a control measurement of a control scattered light intensity distribution,
the control scattered light intensity distribution comprising control incident light scattered by a control sample of cells.
the control sample of cells comprising a control plurality of cells from a sample of cells,
the sample of cells comprising cells from blood of a person infected with at least one variant from a viral plurality of human immunodeficiency virus variants;
causing a treatment signal plurality representing at least a plurality of treatment measurements of a treatment distribution plurality of treatment scattered light intensity distributions,
the treatment distribution plurality comprising treatment incident light scattered respectively from each Ith member of a treatment sample plurality of treatment samples of cells,
each Ith member of the treatment sample plurality comprising an Ith treatment plurality of cells from the sample of cells with an Ith treatment from a treatment plurality of antiviral treatments added;
causing a ranking signal by use of at least the control signal and at least a subset of the treatment signal plurality,
the ranking signal representing at least comparisons between at least some of the subset of the treatment signal plurality and the control signal.
9. The method of claim 8 wherein the step of causing the ranking signal comprises causing the ranking signal to represent at least correlation coefficients between at least some of the subset of the treatment signal plurality paired with the control signal.
10. The method of claim 9 wherein the step of causing the ranking signal also comprises causing the ranking signal to represent comparisons between at least some of the subset of the treatment signal plurality and other members of the treatment signal plurality.
11. The method of claim 9 wherein the step of causing the ranking signal comprises causing the ranking signal to represent correlation coefficients of at least some of the subset of the treatment signal plurality paired with other members of the treatment signal plurality.

Fig. 1

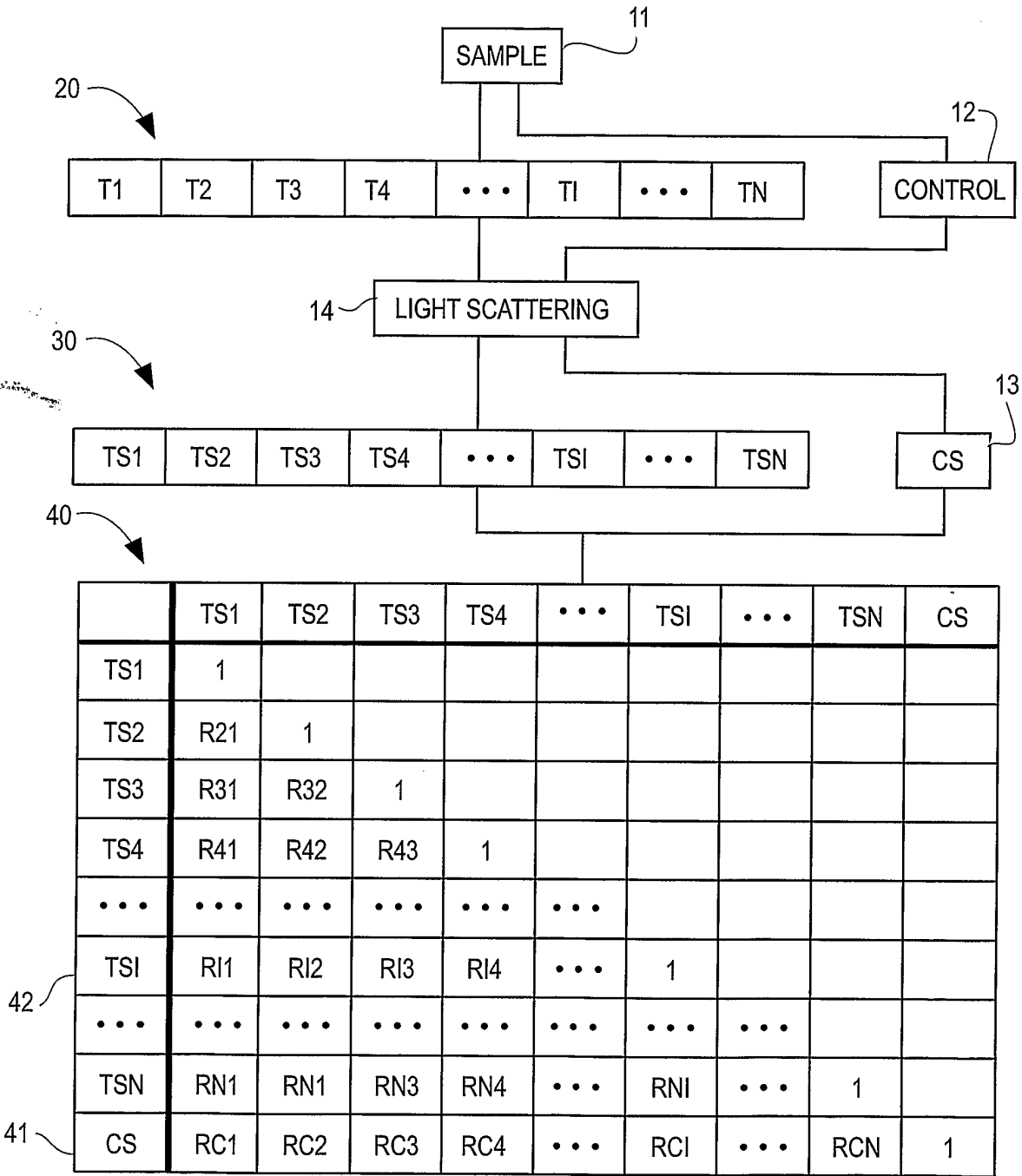


Fig. 2