CLAIMS

1. A matrix-assisted method of analyzing a liquid sample that includes biological materials for one or more target components, comprising:

(a) adding a solidifying agent to a specimen obtained from the liquid sample that includes the biological materials;

(b) generating a solidified sample comprising dispersed biological materials to capture and immobilize the dispersed biological materials in a three-dimensional state;

(c) introducing a refractive index matching material to the solidified sample; and

(d) imaging the solidified sample to identify the one or more target components in the dispersed biological materials;

in which the solidifying agent comprises a mixture of chemical monomers and cross linkers to create a synthetic chemical gel having a chemically cross-linked polymer network.

2. A method according to Claim 1, further comprising (i) labelling the specimen obtained from the liquid sample in step (a) with one or more probes for the one or more target components prior to adding the solidifying agent; and/or (ii) labelling the solidified sample from step (b) with one or more probes for the one or more target components.

3. A method according to Claim 2, in which the labelling comprises contacting the specimen obtained from the liquid sample in step (a) with a molecular probe; and/or contacting the solidified sample from step (b) with a molecular probe in which the molecular probe is an antibody, a fluorescent dye or a nucleic acid probe.

4. A method according to Claim 1, 2 or 3, in which the one or more target components includes a cellular target or an intracellular target.

5. A method according to Claim 1, further comprising introducing an optically cleared gelled solid sample from step (c) into a sample holder that is immersed in a solution that includes a refractive index matching material.

6. A method according to Claim 1, in which the liquid sample is a liquid blood sample.

7. A method according to Claim 6, in which the specimen is obtained from the liquid blood sample by a process that includes removing red blood cells and platelets from the liquid blood sample, and in which the specimen includes peripheral blood mononuclear cells (PBMCs) isolated from the liquid blood sample.

8. A method according to Claim 7, further comprising:

(i) labelling the specimen comprising the isolated PBMCs obtained from the liquid blood sample with one or more probes for one or more rare circulating cells prior to adding the solidifying agent; and/or labelling the matrix-supported sample from step (b) with one or more probes for the one or more rare circulating cells; and

(ii) imaging the optically cleared solidified sample from step (c) to determine the presence of the one or more probes, thereby determining the presence of rare circulating cells in the liquid blood sample.

9. A method according to Claim 8, in which the labelling further comprises adding a probe for white blood cells.

10. A method according to Claim 8 or 9, in which the one or more probes recognizes a cancer specific antigen or a tumor-specific DNA sequence or a tumor-specific RNA sequence.

11. A method according to Claim 8, 9 or 10, in which the one or more probes are selected from an antibody or nucleic acid probe, and more particularly, in which the one or more probes confers detection of one or more of EpCAM, HER2, CDX2, CK20, CK19, PD/PDL-1 and EGFR antigen or corresponding nucleic acid sequence.

12. A method according to any of Claims 8 to 11, in which the one or more rare circulating cells includes a circulating tumor cell.

13. A method according to Claim 8 or 9, in which the one or more rare circulating cells includes a circulating epithelial cell or circulating endothelial cell.

14. A method according to any preceding claim, in which prior to step (a), the biological specimen is subject to a fixation procedure in which the fixation procedure comprises incubating the biological specimen in a fixative solution.

15. A method according to any preceding claim, in which imaging is carried out by fluorescence microscopy, optionally, by light sheet fluorescence microscopy.

16. A method according to Claim 1, further comprising performing delipidation on the solidified sample.