CLAIMS

1. A system for enriching target cells in a sample, the system comprising

a microfluidic chip comprising a sample inlet, a sample outlet, a waste outlet and a microfluidic channel, the sample inlet being coupled to an upstream end of the microfluidic channel and the sample outlet and the waste outlet being coupled to a downstream end of the microfluidic channel, the microfluidic chip being configured such that target cells are directed to the sample outlet and non-target cells are directed to the waste outlet;

a sample input pump configured to introduce the sample into the sample inlet of the microfluidic chip;

a~~n~~ first output flow rate detector configured to measure a flow rate at the sample outlet ~~and /~~ or the waste outlet of the microfluidic chip;

a sample collection switching valve having a configuration switchable between a first configuration in which the sample output of the microfluidic chip is coupled to a sample output container and a second configuration in which the sample output of the microfluidic chip is coupled to a waste output container; and

a controller configured to control the configuration of the sample collection switching valve using the flow rate measured by the first output flow rate detector, wherein the controller is configured to determine a flow ratio between the sample outlet and the waste outlet and further configured to compare the flow ratio with a predetermined range of flow ratios and to switch the sample collection switching valve to the second configuration if the flow ratio is outside the predetermined range of flow ratios, the predetermined range of flow ratio being fixed by controlling resistance of tubing of the sample outlet and the waste outlet.

2. ~~A system according to~~The system of claim 1, wherein the controller is configured to compare the flow rate measured by the first output flow rate detector with a predetermined range of flow rate values, and the controller is further configured to switch the sample collection switching valve to the second configuration if the flow rate measured by the first output flow rate detector is outside the predetermined range of flow rate values.

~~3. A system according to any preceding claim wherein the controller is configured to determine a flow ratio between the sample outlet and the waste outlet and further configured to compare the flow ratio with a predetermined range of flow ratios and to switch the sample collection switching valve to the second configuration if the flow ratio is outside the predetermined range of flow ratios.~~

43. A system according toThe system of claim 31, wherein the controller is configured to determine the flow ratio from the flow rate measured by the first output flow rate detector and a total flow rate through the microfluidic chip.

54. AThe system according toof claim 31, comprising awherein the first output flow rate detector is configured to measure a flow rate at the samplewaste outlet, the system further comprises and a second output flow rate detector configured to measure a flow rate at the wastesample outlet of the microfluidic chip, wherein the controller is configured to determine the flow ratio from a firstthe flow rate measured byat the waste outlet by the first flow rate detector and a secondthe flow rate measured at the sample outlet by the second flow rate detector.

65. A The system according to any precedingof claim 1, wherein the sample comprises a density matching liquid having a density selected such that the target cells are uniformly suspended in the sample during processing.

76. AThe system according to any precedingof claim 1, wherein the microfluidic chip further comprises a diluent inlet coupled to the upstream end of the microfluidic channel and the system further comprise a diluent inlet pump configured to introduce a diluent buffer into the diluent inlet.

8. A system according to claim 7, wherein the diluent buffer comprises an isotonic solution.

9. A system according to claim 7 or claim 8 wherein the diluent buffer comprises a surfactant solution.

107. AThe system according toof any one of claims 7 to 96, further comprising a debubbler arranged to remove bubbles from the diluent buffer.

11. A system according to any preceding claim wherein the sample comprises a blood sample or blood constituents.

128. AThe system according to any precedingof claim 1, wherein the target cells are circulating tumour cells.

~~13~~9. ~~A~~The system ~~according to any preceding~~of claim 1, wherein the microfluidic channel comprises a spiral or curved section.

~~14~~10. A method of enriching target cells in a sample, using a microfluidic chip, the microfluidic chip comprising a sample inlet, a sample outlet, a waste outlet and a microfluidic channel, the sample inlet being coupled to an upstream end of the microfluidic channel and the sample outlet and the waste outlet being coupled to a downstream end of the microfluidic channel, the microfluidic chip being configured such that target cells are directed to the sample outlet and non-target cells are directed to the waste outlet;
the method comprising:

introducing the sample into the sample inlet of the microfluidic chip;

monitoring a flow rate at the sample outlet ~~and /~~ or the waste outlet of the microfluidic chip;

controlling the configuration of a sample ~~switching~~ collection switching valve using the monitored flow rate, the sample collection switching valve having a configuration switchable between a first configuration in which the sample output of the microfluidic chip is coupled to a sample output container and a second configuration in which the sample output of the microfluidic chip is coupled to a waste output container; and

determining a flow ratio between the sample outlet and the waste outlet, comparing the flow ratio with a predetermined range of flow ratios and to switching the sample collection switching valve to the second configuration if the flow ratio is outside the predetermined range of flow ratios, the predetermined range of flow ratio being fixed by controlling resistance of tubing of the sample outlet and the waste outlet.

~~15~~11. ~~A~~The method ~~according to~~of claim ~~14~~10, further comprising suspending the sample in a density matching liquid prior to introducing the sample into the sample inlet of the microfluidic chip, the density matching liquid having a density selected such that the target cells are uniformly suspended in the sample during processing.

~~16~~12. ~~A~~The method ~~according to~~of claim ~~14 or 15~~10, further comprising performing centrifugation and/~~ or~~ blood lysis on the sample before introducing the sample into the sample inlet of the microfluidic chip.

~~17~~13. ~~A~~The method ~~according to any one~~ of claim~~s 14 to 16~~10, further comprising comparing the monitored flow rate with a predetermined range of flow rate values, and switching the sample collection switching valve to the second configuration if the monitored

flow rate ~~measured by the output flow rate detector~~ is outside the predetermined range of flow rate values.

~~18. A method according to any one of claims 14 to 17, further comprising determining a flow ratio between the sample outlet and the waste outlet, comparing the flow ratio with a predetermined range of flow ratios and to switching the sample collection switching valve to the second configuration if the flow ratio is outside the predetermined range of flow ratios.~~

~~19~~14. ~~A~~The method ~~according to~~of claim ~~18~~10, wherein determining the flow ratio comprises determining the flow ratio from the monitored flow rate ~~the sample outlet or the waste outlet of the microfluidic chip~~ and a total flow rate through the microfluidic chip.

~~20~~15 ~~A~~The method ~~according to~~of claim ~~18~~10, wherein the monitored flow rate is the ~~comprising measuring a first flow rate at the sample outlet and a measuring a second~~ flow rate at the waste outlet of the microfluidic chip, the method further comprises measuring a flow rate at the sample outlet, wherein determining the flow ratio comprises determining the flow ratio from the ~~first~~monitored flow rate and the ~~second~~measured flow rate at the sample outlet.

~~21~~16. ~~A~~The method ~~according to any one~~ of claim~~s 14 to 20~~10, wherein the microfluidic chip further comprises a diluent inlet coupled to the upstream end of the microfluidic channel and the method further comprises introducing a diluent buffer into the diluent inlet.

~~22. A method according to claim 21, wherein the diluent buffer comprises an isotonic solution.~~

~~23. A method according to claim 21 or 22, wherein the diluent buffer comprises a surfactant solution.~~

~~24~~17. ~~A~~The method ~~according to any one~~ of claim~~s 21 to 23~~16, further comprising removing bubbles from the diluent buffer before introducing the diluent buffer into the diluent inlet.

~~25. A method according to any one of claims 14 to 24 wherein the sample comprises a blood sample or blood constituents.~~

~~26~~18. ~~A~~The method ~~according to any one~~ of claim~~s 14 to 25~~10, wherein the target cells are circulating tumour cells.

~~27~~19. ~~A~~The method ~~according to any one~~ of claim~~s 14 to 26~~10, wherein the microfluidic channel comprises a spiral or curved section.

~~28~~20. A method of analysing a sample, the method comprising:

enriching target cells in the sample using a method ~~according to any one~~ of claim~~s 14 to 27~~10; and

analysing the enriched target cells for diagnostic use.

~~29. A method according to claim 28 wherein analysing the enriched target cells for diagnostic use comprises detection of intra-cellular and/or extra-cellular protein markers; analysis of cell and nuclear morphology; and/or molecular characterization by sequencing of nucleic acids by next-generation sequencing (NGS) and/or Sanger sequencing, and/or digital polymerase chain reaction (PCR), and/or droplet digital PCR, quantitative PCR (qPCR) and/or fluorescence in-situ hybridization (FISH); and/or copy number variation of nucleic acids of interest.~~