CLAIMS

1. A microfluidic device comprising:

at least one inlet for receiving circulating tumor cells and other cells in a sample;

at least one curvilinear and/or spiral channel through which the sample is caused to undergo migration along at least a partial Dean vortex to isolate the circulating tumor cells from the other cells; ~~and~~

a flow resistance channel arranged to be coupled to the at least one inlet, the flow resistance channel comprising a series of microchannels to stabilise flow fluctuations; and

at least one outlet ~~configured to communicate~~in communication with the at least one curvilinear and/or spiral channel for providing the isolated circulating tumor cells,

wherein the at least one curvilinear and/or spiral channel is configured to provide a predetermined Force ratio greater than or equal to 2 based on a desired threshold cell size of the circulating tumor cells, the predetermined Force ratio being defined as a ratio of inertial lift force (F_L) to Dean drag force (F_D), and wherein the predetermined Force ratio is further defined according to the equation:

$$i_F = F_L / F_D = \frac{85.11 R_C a_C^3}{h^4},$$

where i_F is the Force ratio, R_c is the radius of curvature, a_c is the cell size, and h is the at least one curvilinear and/or spiral channel height, wherein the threshold cell size is about 15-20 µm.

2. The device of claim 1, wherein the device includes ~~being arranged as~~is comprised in a biochip in a microfluidic packaging configured as a disposable cartridge.

3. The device of claim 1~~ or 2~~, wherein the at least one curvilinear and/or spiral channel height is arranged to be smaller than ten times the threshold cell size.

~~4. The device of any preceding claim, wherein the channel includes a radius of curvature which is configured to further provide the predetermined Force ratio.~~

~~5. The device of any preceding claim, wherein the channel includes a hydraulic diameter which is configured to further provide the predetermined Force ratio.~~

~~6~~4. The device of claim ~~5~~1, wherein the at least one curvilinear and/or spiral channel has a cross-section having~~hydraulic diameter is defined by~~ a channel width and a channel height ~~forming~~defining an aspect ratio of the at least one curvilinear and/or spiral channel.

~~7~~5. The device of claim ~~6~~4, wherein the at least one curvilinear and/or spiral channel width is arranged to be approximately between 300 µm to 650 µm.

~~8~~6. The device of claim ~~7~~5, wherein the at least one curvilinear and/or spiral channel height is arranged to be approximately between 120 µm to 180 µm.

~~9. The device of any preceding claim, wherein the predetermined Force ratio is defined as a ratio of inertial lift force to Dean drag force.~~

~~10. The device of claim 9, wherein the predetermined Force ratio is further defined according to the equation: $i_F = F_L/F_D = \frac{85.11R_C a_C^3}{D_H^4} = \frac{85.11R_C a_C^3}{h^4}$, where i_F is the Force ratio, R_c is the radius of curvature, a_c is the cell size, D_H is the hydraulic diameter and h is the microchannel height.~~

~~11. The device of any preceding claim, wherein the predetermined Force ratio has a value equal to or greater than 2.~~

~~12~~7. The device of claim ~~4~~1, wherein the radius of curvature is configured to be approximately between 5 mm to 20 mm.

~~13~~8. The device of ~~any preceding~~ claim 1, wherein at least one outlet includes a first outlet and a second outlet to respectively enable the isolated circulating tumor cells and the other cells to be provided.

~~14~~9. The device of ~~any preceding~~ claim 1, wherein a total length of the at least one curvilinear and/or spiral channel is arranged to be between 5 cm to 100 cm.

~~15. The device of any preceding claim, wherein the sample is a whole blood sample or a red blood cell depleted blood sample.~~

~~16. The device of any preceding claim, wherein the circulating tumor cells are caused to migrate from one side of the channel to an opposing side during at least partial Dean vortex.~~

~~17. The device of any preceding claim, wherein the at least one inlet includes a first and a second inlet arranged to be coupled to respective damper chambers to regulate a flow rate of the sample through the channel, wherein the first inlet is for introducing the sample into the channel and the second inlet is for introducing a sheath fluid into the channel.~~

~~18~~10. The device of ~~any preceding~~ claim 9, wherein the at least one curvilinear and/or spiral channel is an arc and the total length is configured to generate a half dean ~~vortex~~cycle migration.

~~19~~11. The device of ~~any preceding~~ claim 9, wherein the at least one curvilinear and/or spiral channel is a spiral and the total length is configured to generate whole number multiples of a dean ~~vortex~~cycle migration.

~~20~~12. The device of ~~any proceeding~~ claim 1, wherein the at least one inlet includes a first inlet and a second inlet arranged to be coupled to respective damper chambers to regulate a flow rate of the sample in the at least one curvilinear and/or spiral channel, wherein the first inlet is for introducing the sample into the at least one curvilinear and/or spiral channel and the second inlet is for introducing a sheath fluid into the at least one curvilinear and/or spiral channel~~further includes a flow resistance channel arranged to be coupled to any of the inlets~~.

13. A diagnostic system configured for detecting circulating tumor cells in a sample comprising:

a microfluidic device according to claim 1 configured to isolate the circulating tumor cells from other biological cells in a sample; and

a processor configured to generate a diagnostic indication based on the circulating tumor cells isolated by the microfluidic device.

14. A diagnostic system according to claim 13, wherein the sample is a whole blood sample or a red blood cell depleted blood sample.

~~21~~15. A method of manufacturing a microfluidic device ~~comprises~~comprising:

providing at least one inlet for receiving circulating tumor cells and other cells in a sample, and at least one curvilinear and/or spiral channel through which the sample is caused to undergo migration along at least a partial Dean vortex to isolate the circulating tumor cells from the other cells;

providing a flow resistance channel arranged to be coupled to the at least one inlet, the flow resistance channel comprising a series of microchannels to stabilise flow fluctuations;

providing at least one outlet configured for communicating with the at least one curvilinear and/or spiral channel for providing the isolated circulating tumor cells; and

selecting a curvilinear and/or spiral channel height, radius of curvature, and length ~~and flow rate~~ to provide a predetermined Force ratio greater than or equal to 2 based on a desired threshold cell size of the circulating tumor

cells, the predetermined Force ratio being defined as a ratio of inertial lift force (F_L) to Dean drag force (F_D), and wherein the predetermined Force ratio is further defined according to the equation:

$$i_F = F_L / F_D = \frac{85.11 R_C a_C^3}{h^4},$$

where i_F is the Force ratio, R_c is the radius of curvature, a_c is the cell size, and h is the curvilinear and/or spiral channel height, wherein the threshold cell size is about 15-20 µm.

~~22. The method of claim 21, further comprising selecting a hydraulic diameter of the channel to further provide the predetermined Force ratio.~~

~~23. The method of claim 22, further comprising selecting a fluid velocity to further provide the predetermined Force ratio.~~

~~24. A diagnostic system configured for detecting circulating tumor cells in a sample comprising:~~

~~a microfluidic device according to any of claims 1 to 20 configured to isolate the circulating tumor cells from other biological cells in the sample; and~~

~~a processor configured to generate a diagnostic indication based on the circulating tumor cells isolated by the microfluidic device.~~

~~25. The system of claim 24, further includes a flow regulator for adjusting a fluid velocity of the sample flowing through the microfluidic device.~~