CLAIMS

1. A microfluidic device for separating metaphase chromosomes in a metaphase chromosome-containing fluid, the microfluidic device including:

a flow channel including:

an inlet to receive a fluid including metaphase chromosomes;

an outlet to discretely dispense individual metaphase chromosomes;

a series of expanded regions; and

one or more constrictions located between consecutive expanded regions in the series of expanded regions;

wherein the constrictions are operable to apply sufficient shear stress to separate the metaphase chromosomes from one another; and

the expanded regions are operable to disperse chromosomes from one another.

2. A microfluidic device for separating metaphase chromosomes in a metaphase chromosome-containing fluid, the microfluidic device including:

a flow channel having a width of from about 10 μm to about 30 μm, the flow channel including:

an inlet;

an outlet; and

a series of expanded regions, and one or more constrictions located between consecutive expanded regions in the series of expanded regions;

wherein the plurality of expanded regions have a channel width of from about 50 μm to about 150 μm, and each constriction in the plurality of constrictions has a minimum width of from about 1 μm to about 3 μm.

3. The microfluidic device of claim 1 or claim 2, wherein the flow channel has a depth of from about 5 μm up to about 40 μm.

4. The microfluidic device of any one of the preceding claims, wherein the length of the flow channel is from about 2 mm to about 15 mm.

5. The microfluidic device of any one of the preceding claims, wherein each successive constriction from the inlet to the outlet has a smaller minimum width than a preceding constriction.

6. The microfluidic device of any one of the preceding claims, wherein one or more of the one or more constrictions has a widening tapered outlet.

7. The microfluidic device of any one of the preceding claims, wherein each of the expanded regions in the series of expanded regions has substantially the same width.

8. The microfluidic device of any one of the preceding claims, wherein the series of expanded regions includes at least 3 expanded regions and up to 20 expanded regions.

9. The microfluidic device of any one of the preceding claims, wherein the flow channel includes more than one constriction between each expanded region in the series of expanded regions.

10. The microfluidic device of any one of the preceding claims, wherein the inlet has a width of from 2 μm to 3 μm.

11. The microfluidic device of any one of the preceding claims, wherein the microfluidic device further includes cell capture and lysis structure upstream of the inlet, the cell capture and lysis structure including:

a cell trap adjacent the flow channel inlet configured to receive and retain a cell from a fluid sample including the cell, the cell trap including:

a viewing element to permit inspection of the cell; and

an opening connected to the flow channel inlet via a passage, the opening and passage sized to impede passage of the cell therethrough;

a lysis port configured to introduce a lysis buffer to the cell trap.

12. The microfluidic device of claim 11, wherein the size of the opening is from about 10 µm to 20 µm and a width of the passage is from about 2 µm to about 3 µm.

13. The microfluidic device of any one of the preceding claims, wherein the cell trap is a rectangular prism shaped hollow formation in the microfluidic device with an open face to permit entry of a cell into the cell trap.

14. The microfluidic device of any one of the preceding claims, further including a chromosome dispensing structure downstream of the outlet, the chromosome dispensing structure including:

a dispensing channel defined between a channel inlet and a channel outlet, and having a port for receiving an individual chromosome from the outlet of the flow channel;

wherein the channel outlet is connected to a dispensing tube configured to dispense single chromosomes from the microfluidic device in the form of a fluid droplet including the single chromosome.

15. A method for separating metaphase chromosomes in a metaphase chromosome-containing fluid, the method including:

passing the metaphase chromosome-containing fluid through the microfluidic device of any one of the preceding claims at a pressure whereby the constrictions subject the metaphase chromosomes to sufficient shear stress to separate the metaphase chromosomes from one another.

16. A method for separating metaphase chromosomes in a chromosome-containing fluid, the method including:

passing a chromosome-containing fluid including metaphase chromosomes through a microfluidic device, the microfluidic device having a flow channel including:

a plurality of expanded regions located between an inlet and an outlet; and

one or more constrictions located between one or more of the expanded regions;

subjecting metaphase chromosomes, at or in the one or more constrictions, to sufficient shear stress to separate the metaphase chromosomes from one another;

dispersing the separated metaphase chromosomes in the plurality expanded regions from one another.

17. A method for separating metaphase chromosomes in a chromosome-containing fluid with a microfluidic device, the method including:

passing the fluid through a flow channel of a microfluidic device, the flow channel having a plurality of alternating constrictions and expansions;

wherein when the fluid is passed through a constriction, the method includes applying a pressure pulse to subject the metaphase chromosomes to a shear stress sufficient to separate the metaphase chromosomes from one another;

wherein when the fluid is passed through an expansion, the microfluidic device is operated at a pressure to disperse the separated chromosomes from one another.

18. The method of any one of claims 15 to 17, wherein the shear stress is from at least about 0.02 N/m^2 to at least about 15,000 N/m^2 as measured at walls of the minimum width of the constriction.

19. The method of any one of claims 15 to 18, wherein the method initially includes:

trapping a metaphase cell in a cell trap of the microfluidic device; and

introducing a lysis buffer to the metaphase cell and applying a pressure pulse to drive the metaphase cell from the cell trap and into the flow channel under sufficient shear stress to lyse the cell and provide the chromosomes in the chromosome-containing fluid.

20. The method of any one of claims 15 to 19, further including:

receiving the dispensed individual chromosomes from the outlet of the flow channel into a dispensing channel of the microfluidic device;

transporting the individual chromosomes to a dispensing tube; and

dispense single chromosomes from the microfluidic device via the dispensing tube in the form of a fluid droplet including the single chromosome.

CLAIMS

1. A microfluidic device for separating metaphase chromosomes in a metaphase chromosome-containing fluid and individually dispensing separated metaphase chromosomes, the microfluidic device including:

a flow channel including:

an inlet to receive a fluid including metaphase chromosomes;

an outlet to discretely dispense individual metaphase chromosomes;

a series of expanded regions; and

one or more constrictions located between consecutive expanded regions in the series of expanded regions;

wherein the constrictions are operable to apply sufficient shear stress to separate the metaphase chromosomes from one another; and

the expanded regions are operable to disperse chromosomes from one another.

2. A microfluidic device for separating metaphase chromosomes in a metaphase chromosome-containing fluid, the microfluidic device including:

a flow channel, the flow channel including:

an inlet;

an outlet; and

a series of expanded regions, and one or more constrictions located between consecutive expanded regions in the series of expanded regions;

wherein the plurality of expanded regions have a channel width of from 50 μm to 150 μm, and each constriction in the plurality of constrictions has a minimum width of from 1 μm to 3 μm;

wherein the flow channel has a width of from 10 μm to 30 μm in regions other than the expanded regions and the constrictions.

3. The microfluidic device of claim 1 or claim 2, wherein the flow channel has a depth of from 5 μm up to 40 μm.

4. The microfluidic device of any one of the preceding claims, wherein the length of the flow channel is from 2 mm to 15 mm.

5. The microfluidic device of any one of the preceding claims, wherein each successive constriction from the inlet to the outlet has a smaller minimum width than a preceding constriction.

6. The microfluidic device of any one of the preceding claims, wherein one or more of the one or more constrictions has a widening tapered outlet.

7. The microfluidic device of any one of the preceding claims, wherein each of the expanded regions in the series of expanded regions has substantially the same width.

8. The microfluidic device of any one of the preceding claims, wherein the series of expanded regions includes at least 3 expanded regions and up to 20 expanded regions.

9. The microfluidic device of any one of the preceding claims, wherein the flow channel includes more than one constriction between each expanded region in the series of expanded regions.

10. The microfluidic device of any one of the preceding claims, wherein the inlet has a width of from 2 μm to 3 μm.

11. The microfluidic device of any one of the preceding claims, wherein the microfluidic device further includes cell capture and lysis structure upstream of the inlet, the cell capture and lysis structure including:

a cell trap adjacent the flow channel inlet configured to receive and retain a cell from a fluid sample including the cell, the cell trap including:

a viewing element to permit inspection of the cell; and

an opening connected to the flow channel inlet via a passage, the opening and passage sized to impede passage of the cell therethrough;

a lysis port configured to introduce a lysis buffer to the cell trap.

12. The microfluidic device of claim 11, wherein the size of the opening is from 10 µm to 20 µm and a width of the passage is from 2 µm to 3 µm.

13. The microfluidic device of claim 11 or claim 12, wherein the cell trap is a rectangular prism shaped hollow formation in the microfluidic device with an open face to permit entry of a cell into the cell trap.

14. The microfluidic device of any one of the preceding claims, further including a chromosome dispensing structure downstream of the outlet, the chromosome dispensing structure including:

a dispensing channel defined between a channel inlet and a channel outlet, and having a port for receiving an individual chromosome from the outlet of the flow channel;

wherein the channel outlet is connected to a dispensing tube configured to dispense single chromosomes from the microfluidic device in the form of a fluid droplet including the single chromosome.

15. A method for separating metaphase chromosomes in a metaphase chromosome-containing fluid, the method including:

passing the metaphase chromosome-containing fluid through the microfluidic device of any one of the preceding claims at a pressure whereby the constrictions subject the metaphase chromosomes to sufficient shear stress to separate the metaphase chromosomes from one another.

16. A method for separating metaphase chromosomes in a chromosome-containing fluid, the method including:

passing a chromosome-containing fluid including metaphase chromosomes through a microfluidic device, the microfluidic device having a flow channel including:

a plurality of expanded regions located between an inlet and an outlet; and

one or more constrictions located between one or more of the expanded regions;

subjecting metaphase chromosomes, at or in the one or more constrictions, to sufficient shear stress to separate the metaphase chromosomes from one another;

dispersing the separated metaphase chromosomes in the plurality expanded regions from one another.

17. A method for separating metaphase chromosomes in a chromosome-containing fluid with a microfluidic device, the method including:

passing the fluid through a flow channel of a microfluidic device, the flow channel having a plurality of alternating constrictions and expansions;

wherein when the fluid is passed through a constriction, the method includes applying a pressure pulse to subject the metaphase chromosomes to a shear stress sufficient to separate the metaphase chromosomes from one another;

wherein when the fluid is passed through an expansion, the microfluidic device is operated at a pressure to disperse the separated chromosomes from one another.

18. The method of any one of claims 15 to 17, wherein the shear stress is from at least 0.02 N/m^2 to at least 15,000 N/m^2 as measured at walls of the minimum width of the constriction.

19. The method of any one of claims 15 to 18, wherein the method initially includes:

trapping a metaphase cell in a cell trap of the microfluidic device; and

introducing a lysis buffer to the metaphase cell and applying a pressure pulse to drive the metaphase cell from the cell trap and into the flow channel under sufficient shear stress to lyse the cell and provide the chromosomes in the chromosome-containing fluid.

20. The method of any one of claims 15 to 19, further including:

receiving the dispensed individual chromosomes from the outlet of the flow channel into a dispensing channel of the microfluidic device;

transporting the individual chromosomes to a dispensing tube; and

dispense single chromosomes from the microfluidic device via the dispensing tube in the form of a fluid droplet including the single chromosome.