Claims:

1. A method of producing a sample enriched for activated T lymphocytes using a microfluidic device, the microfluidic device comprising a flow path having a first region comprising a first array of posts, the method comprising:

flowing a fluid sample comprising a mixture of activated and resting T lymphocytes through the first region of the flow path of the microfluidic device, wherein:

the direction of fluid flow in the first region of the flow path defines a first direction;

the posts in the first array are arranged in rows and columns;

the rows of posts in the first array define a first array direction that differs from the first direction of the first region by a tilt angle (ε), and the columns of posts in the first array repeat periodically with a periodicity equal to $1/\varepsilon$, wherein ε is measured in radians;

adjacent posts in each respective column in the first array are separated by gaps through which fluid of the fluid sample can flow generally transversely with respect to the columns, wherein a majority of the gaps have a characteristic size that corresponds to a primary gap size of the first array, and

the first array is characterized by a critical size (D_c) of about 4 microns to about 10 microns.

2. The method of claim 1, wherein the first region of the flow path is a defined by a main channel having a width, and wherein the first array of posts extends across the entire width of the main channel,

wherein the first array is characterized by a D_c of about 4 microns to about 7 microns,

wherein the first array has a tilt angle ε of about 1/5 radians to about 1/30 radians,

wherein the primary gap size of the first array is about 15 microns to about 40 microns, and

wherein the posts of the first array have a diameter of about 30 microns to about 100 microns.

3. The method of claim 1 or 2, wherein the posts of the first array have a rounded shape in cross-section or a polygonal shape in cross-section.

4. The method of claim 3, wherein the posts of the first array all have the same orientation, and wherein the orientation is such that no axis of symmetry in the cross-sectional shape of the posts is parallel to an axis defined by the first direction.

5. The method of any one of claims 1 to 4, wherein the flow path of the microfluidic device comprises a second region configured to receive the fluid sample after the fluid sample passes through the first region of the microfluidic device, the second region having a divider that separates the second region into a first channel that receives a first portion of the fluid sample and a second channel that receives a second portion of the fluid sample, and

wherein the divide of the second region is positioned such T lymphocytes having a diameter greater than D_c are enriched, relative to the fluid sample, in the second portion of the fluid sample.

6. The method of claim 5, wherein T lymphocytes having a $CD8^+$, CD45 RO^+/RA^-, $CCR7^-$, $CD62L^-$ phenotype and/or a $CD8^+$, CD45 RO^+/RA^-, $CCR7^+$, $CD62L^-$ phenotype are enriched in the second portion of the fluid sample.

7. The method of any one of claims 1 to 6, wherein the fluid sample is flowed through the first region of the flow path at a rate of about 0.01 microliters/second to about 10 microliters/second.

8. The method of claim 5 or 6, wherein the second channel comprises a first sub-region comprising a second array of posts, wherein flowing the fluid sample through the first region of the flow path causes the second portion of the fluid sample, along with any cells contained therein, to flow through the second array of posts in the first sub-region, and further wherein:

the direction of fluid flow in the first sub-region of the second channel defines a second direction;

the posts in the second array are arranged in rows and columns;

the rows of posts in the second array define a second array direction that differs from the second direction by a tilt angle (ε'), and the columns of posts in the second array repeat periodically with a periodicity equal to $1/\varepsilon'$, wherein ε' is measured in radians;

adjacent posts in each respective column in the second array are separated by gaps through which fluid of the second portion of the fluid sample can flow generally transversely with respect to the columns, wherein a majority of the gaps have a characteristic size that corresponds to a secondary gap size of the second array, and

the second array is characterized by a critical size (D_c) of about 4 microns to about 10 microns.

9. The method of claim 8, wherein the second channel has a width, and wherein the second array of posts extends across the entire width of the second channel,

wherein the second array has a tilt angle ε' of about 1/5 radians to about 1/30 radians,

wherein the secondary gap size of the second array is about 15 microns to about 40 microns, and

wherein the posts of the second array have a diameter of about 30 microns to about 100 microns.

10. The method of claim 8 or 9, wherein the second array of posts is characterized by a D_c of about 7 microns to about 10 microns.

11. The method of any one of claims 8 to 10, wherein the second channel comprises a second sub-region configured to receive the second portion of the fluid sample after it passes through the first sub-region, the second sub-region having a divide

that separates the second channel into a third channel that receives a first sub-portion of fluid from the second portion of the fluid sample and a fourth channel that receives a second sub-portion of fluid from the second portion of the fluid sample, and

wherein the divide of the second sub-region is positioned such that T lymphocytes having a diameter greater than D_c are enriched, relative to the second portion of the fluid sample, in the second sub-portion of fluid.

12. The method of claim 11, wherein the first sub-portion of fluid comprises at least 50% of the second portion of the fluid sample.

13. The method of any one of claims 1 to 12, wherein the fluid sample is a peripheral blood sample obtained from a subject or a sample derived therefrom.

14. The method of claim 13, wherein the fluid sample is a peripheral blood sample that has been depleted at least one non-T lymphocyte cell type.

15. The method of claim 13, wherein the fluid sample is a peripheral blood sample that has been enriched for $CD8^+$ T lymphocytes.

16. The method of claim 15, wherein the fluid sample has been depleted of effector T lymphocytes (T_{EFF}) and/or memory T lymphocytes (T_{CM}).

17. The method of claim 15, wherein the fluid sample has been enriched for naïve T lymphocytes ($T_{naïve}$) or cells having a $CD45RA^+$ phenotype.

18. The method of claim 15, wherein the fluid sample has been enriched for central memory T lymphocytes (T_{CM}) or cells having a $CD45RO^+$ phenotype in combination with a $CCR7^+$ and/or $CD62L^+$ phenotype.

19. The method of claim 13, further comprising:

obtaining a sample of peripheral blood or a sample derived therefrom, wherein the peripheral blood originates from a human subject; and

generating the fluid sample from the sample of peripheral blood or the sample derived therefrom.

20. The method of claim 19, wherein generating the fluid sample comprises:

depleting the peripheral blood sample, or the sample derived therefrom, of at least one non-T lymphocyte cell type; and/or

enriching the peripheral blood sample, or the sample derived therefrom, for $CD8^+$ T lymphocytes.

21. The method of any one of claims 1 to 20, further comprising:

contacting the T lymphocytes in the fluid sample with an activating agent.

22. The method of claim 21, wherein the T lymphocytes in the fluid sample are contacted with the activating agent for a period of at least 48 hours prior to flowing the fluid sample through the first region of the flow path of the microfluidic device.

23. The method of claim 21 or 22, wherein the activating agent comprises artificial antigen presenting cells (aAPCs), and wherein the aAPCs comprise MHC Class I molecules that are complexed with an antigenic peptide.

24. The method of claim 23, wherein the aAPCs further comprise a CD28 agonist.

25. The method of claim 23 or 24, wherein the antigenic peptide is identified in or isolated from a bacterial pathogen, a fungal pathogen, a parasitic pathogen, a viral pathogen, or tumor cells

26. The method of any one of claims 7 to 25, further comprising:

selectively exporting a population of T lymphocytes from the second channel of the flow path of the microfluidic device, wherein the population of T lymphocytes is exported separately from any cells or T lymphocytes that have flowed through the first channel of the flow path of the microfluidic device.

27. The method of any one of claims 1 to 12 and 26, wherein the microfluidic device comprises an inner surface that comprises a coating material.

28. The method of claim 27, wherein the coating material comprises carboxylic acid moieties, saccharide moieties, or polyethylene glycol (PEG) moieties.

29. The method of any one of claims 1 to 12, wherein flowing the fluid sample through the first region of the flow path of the microfluidic device produces a sorted sample that is enriched in activated T lymphocytes, and wherein the enrichment is at least 2-fold.

30. A microfluidic device comprising:

a flow path having a first region comprising a first array of posts, wherein:

the first region comprises a first lateral wall and a second lateral wall which together define a general direction of fluid flow in the first region of the flow path, the general direction corresponding to a fist direction of the first region;

the posts in the first array are arranged in rows and columns;

the rows of posts in the first array define a first array direction that differs from the first direction of the first region by a tilt angle (ε), and the columns of posts in the first array repeat periodically with a periodicity equal to $1/\varepsilon$, where ε is measured in radians;

adjacent posts in each respective column in the first array are separated by gaps through which fluid of a fluid sample can flow generally transversely with respect to the columns, wherein a majority of the gaps have a characteristic size that corresponds to a primary gap size of the first array, and

the first array is characterized by a critical size (D_c) of about 4 microns to about 10 microns.

31. The device of claim 30, wherein the first region of the flow path is a main channel having a width defined by the first and second lateral walls, and wherein the first array of posts extends across the entire width of the main channel,

wherein the first array is characterized by a D_c of about 4 microns to about 7 microns,

wherein the first array has a tilt angle ε of about 1/5 radians to about 1/30 radians,

wherein the primary gap size of the first array is about 15 microns to about 40 microns, and

wherein the posts of the first array have a diameter of about 30 microns to about 100 microns.

32. The device of claim 30 or 31, wherein the columns of the first array are arranged transversely with respect to the first direction of the first region.

33. The device of any one of claims 30 to 32, wherein the posts of the first array have a rounded shape in cross-section or a polygonal shape in cross-section.

34. The device of claim 33, wherein the posts of the first array all have the same orientation, and wherein the orientation is such that no axis of symmetry in the cross-sectional shape of the posts is parallel to an axis defined by the first direction.

35. The device of any one of claims 30 to 34, wherein all gaps between adjacent posts in the columns of the first array are equal to the primary gap size of the first array with the exception that the size of the gaps between adjacent posts of the same column that are most proximal to either the first or second lateral walls may deviate from the primary gap size, and wherein the deviations in gap sizes between posts in the first array reduce boundary irregularities in the flow of a fluid sample through the first array otherwise caused by the first and second lateral walls.

36. The device of any one of claims 30 to 35, wherein the flow path of the microfluidic device comprises a second region configured to receive a fluid sample after the fluid sample passes through the first region of the microfluidic device, the second region having a divide that separates the second region into a first channel that receives a first portion of the fluid sample and a second channel that receives a second portion of the fluid sample.

37. The device of claim 36, wherein the first portion of the fluid sample comprises about 85% to about 95% of the fluid sample.

38. The device of claim 36 or 37, wherein the first channel comprises a first length and the second channel comprises a second length, and wherein the second channel is at least 5 times longer than the first length of the first channel.

39. The device of any one of claims 30 to 38, wherein the first region has a length of about 5 mm to about 15 mm.

40. The device of any one of claims 36 to 39, wherein the second channel comprises a first sub-region comprising a second array of posts, wherein flowing the fluid sample through the first region of the flow path causes the second portion of the fluid sample, along with any cells contained therein, to flow through the second array of posts in the first sub-region of the second channel, and further wherein:

the general direction of fluid flow in the first sub-region of the second channel defines a second direction;

the posts in the second array are arranged in rows and columns;

the rows of posts in the second array define a second array direction that differs from the second direction by a tilt angle (ε'), and the columns of posts in the second array repeat periodically with a periodicity equal to $1/\varepsilon'$, wherein ε' is measured in radians;

adjacent posts in each respective column in the second array are separated by gaps through which fluid of the second portion of the fluid sample can flow generally transversely with respect to the columns, wherein a majority of the gaps have a characteristic size that corresponds to a secondary gap size of the second array, and

the second array is characterized by a critical size (D_c) of about 4 microns to about 10 microns.

41. The device of claim 40, wherein the second channel has a width, and wherein the second array of posts extends across the entire width of the second channel,

wherein the second array has a tilt angle ε' of about 1/5 radians to about 1/30 radians,

wherein the secondary gap size of the second array is about 15 microns to about 40 microns, and

wherein the posts of the second array have a diameter of about 30 microns to about 100 microns.

42. The device of claim 40 or 41, wherein the posts of the second array have a rounded shape in cross-section or a polygonal shape in cross-section, and

wherein the posts of the second array all have the same orientation, and

wherein the orientation is such that no axis of symmetry in the cross-sectional shape of the posts is parallel to an axis defined by the second direction.

43. The device of any one of claims 40 to 42, wherein the second channel comprises a second sub-region configured to receive the second portion of the fluid sample after it passes through the first sub-region, the second sub-region having a divide that separates the second channel into a third channel that receives a first sub-portion of fluid from the second portion of the fluid sample and a fourth channel that receives a second sub-portion of fluid from the second portion of the fluid sample,

wherein the divide of the second sub-region is positioned such that T lymphocytes having a diameter greater than D_c are enriched, relative to the second portion of the fluid sample, in the second sub-portion of fluid.

44. The device of any one of claims 30 to 43, wherein the microfluidic device comprises at least one inner surface that comprises a coating material.

45. The device of claim 44, wherein the coating material comprises carboxylic acid moieties, saccharide moieties, or polyethylene glycol (PEG) moieties.

46. A composition comprising T lymphocytes sorted according to the methods of claim 17, wherein the T lymphocytes are obtained by exporting cells from the second channel of the flow path of the microfluidic device, wherein the population of T lymphocytes is exported separately from any cells or T lymphocytes that have flowed through the first channel of the flow path of the microfluidic device.

47. The composition of claim 46 for use in medicine.

48. Use of a composition of claim 46 in the preparation of a medicament for treating a pathogenic disorder or cancer.