What is claimed herein is:

1. A cell culture system comprising:

a fluidic device having a fluid channel connected to a fluid source, the fluid source supplying fluid to the fluid channel;

a membrane positioned within the channel between membrane support elements, at least portion of the membrane being flexible;

a membrane strain mechanism coupled to the membrane support elements capable of moving the membrane support elements and causing the membrane to stretch along at least one dimension of the membrane; and

at least one layer of intestinal epithelial cells attached to at least one surface of the membrane.

wherein the shear stress on the fluid flowing through the fluid channel is less than 1.0 dyne/cm^2.

2. The system of claim 1, wherein the shear stress on the fluid flowing through the fluid channel is from 0.008 to 0.08 dyne/cm^2.

3. The system of any of claims 1-2, wherein the shear stress on the fluid flowing through the fluid channel is approximately 0.018 dyne/cm^2.

4. The system of any of claims 1-3, wherein the shear stress on the fluid flowing through the fluid channel can vary over time.

5. The system of claim 4, wherein the shear stress on the fluid flowing through the fluid channel can vary over time from 0 to 1000 dyne/cm^2.

6. The system of any of claims 4-5, wherein the shear stress on the fluid flowing through the fluid channel can vary over time from 0.008 to 0.08 dyne/cm^2.

7. The system of any of claims 1-6, wherein the membrane is caused to stretch from 0% to 50%.

8. The system of any of claims 1-6, wherein the membrane is caused to stretch from 5% to 15%.

9. The system of any of claims 1-8, wherein the membrane is caused to stretch approximately 10%.

10. The system of any of claims 1-9, wherein the membrane is caused to stretch more than 15% to create an abnormal condition/state of the intestinal epithelial cells.

11. The system of any of claims 1-10, wherein the membrane is caused to stretch in a cyclic manner at a rate in the range of 0.01 Hz to 2 Hz.

12. The system of any of claims 1-11, wherein the membrane is caused to stretch in a cyclic manner at a rate in the range of 0.05 Hz to 0.25 Hz.

13. The system of any of claims 1-12, wherein the membrane is caused to stretch in a cyclic manner at a rate of 0.15 Hz.

14. The system of any of claims 1-12, wherein the membrane is caused to stretch in a cyclic manner at a rate greater than 0.2 Hz to create an abnormal condition/state of the intestinal epithelial cells.

15. The system of any of claims 1-14, wherein the membrane is caused to stretch in an irregular or intermittent manner.

16. The system of any of claims 1-15, wherein the fluid flows through the fluid channel at a flow rate less than 500 μL/hr.

17. The system of any of claims 1-16, wherein the fluid flows through the fluid channel at a flow rate less than 100 μL/hr.

18. The system of any of claims 1-17, wherein the fluid flows through the fluid channel at a flow rate from 0 to 50 μL/hr.

19. The system of any of claims 1-18, wherein the fluid flows through the fluid channel at a flow rate of approximately 30 μL/hr.

20. The system of any of claims 1-19, further comprising at least one type of attachment molecule that supports adhesion of a plurality of living cells coating at least one side of the membrane.

21. The system of claim 20, wherein the at least one attachment molecule is selected from the group consisting of:

collagen; collagen type I; MATRIGEL™; extracellular matrix; laminin; proteoglycan; vitronectin; fibronection; poly-D-lysine; polypeptides; oligonucleotides; DNA; and polysaccharide.

22. The system of any of claims 1-21, wherein the intestinal epithelial cells are mammalian or human cells.

23. The system of any of claims 1-22, wherein the intestinal epithelial cells are selected from the group consisting of:

Caco2 cells; HT-29 cells; primary small intestine epithelial cells; primary large intestine epithelial cells; iPS cells; ESC cells; stem cells; paneth cells; crypt cells; and mucus-secreting cells.

24. The system of any of claims 1-23, wherein the intestinal epithelial cells of the system further comprise villi structures.

25. The system of any of claims 1-24, wherein the system further comprises at least one layer of endothelial cells on at least the second surface of the membrane.

26. The system of any of claims 1-25, wherein the membrane is positioned such that it divides the fluid channel into a first cell culture channel and a second cell culture channel.

27. The system of Claim 26, wherein the first cell culture channel comprises intestinal epithelial cells.

28. The system of any of Claims 26-27, wherein the second cell culture channel comprises cells selected from the group consisting of:

endothelial cells, immune cells, and connective tissue cells.

29. The system of any of Claims 1-27, wherein the system further comprises microbial cells or pathogens.

30. The system of Claim 29, wherein the microbial cells are maintained in the system for at least 1 day.

31. The system of any of Claims 29-30, wherein the microbial cells are selected from the group consisting of:

Lactobacillus; Bacterioides; Ruminococcus; Peptococcus; Peptostreptococcus; Bifidobacterium; Escherichia; Achromobacter; *Acidaminococcus fermentans; Acinetobacter cacoaceticus*; Aeromonas; *Alcaligenes faecalis*; Bacillus; *Butyriviberio fibrosolvens*; Camplyobacter; *Campylobacter coli; Clostridium difficile; Clostridium sordelli*; *Enterobacter cloacae; Enterococcus faecalis; Enterococcus faecium; Escherichia coli*; Flavobacterium; Mycobacterium; Mycoplasma; *Plesiomonas shigelloides*; *Propionibacterium acnes*; *Pseudomonas aeruginosa*; *Ruminococcus bromii*; Sarcina; *Staphylococcus aureus*; *Streptococcus anginosus;* Veillonella; Vibrio; *Yersinia enterocolitica; Lactobacillus rhamnosus; Lactobacillus rhamnosus* GG; *Bifidobacterium breve; Bifidobacterium longum; Bifidobacterium infantis; Lactobacillus acidophilus; Lactobacillus plantarum; Lactobacillus paracasei; Lactobacillus bulgaricus*; and *Streptococcus thermophilus.*

32. The system of any of Claims 29-30, wherein the microbial cells are pathogenic.

33. The system of Claims 29 or 32, wherein the pathogens are selected from the group consisting of:

enterotoxigenic *Escherichia coli*; *Bilophila wadsworthia;* Shigella; Yersinia; Pleisiomonas; Vibrio; Aeromonas; Campylobacter; Crytosporidia; Coccidosis; Salmonella; *Helicobacter*

pylori; *Clostridium difficile*; *Salmonella kedougou*; Bacteroides; Clostridium; Firmicutes; *Shigellia dysenteriae*; *Salmonella enterica*; *Salmonella typhi;* Listeria; *Listeria monocytogenes; Vibrio parahaemolyticus*; Proteus; *Vibrio cholerae; Enterococcus faecalis; Yersinia enterocolitica;* and *Campylobacter jejuni;* rotavirus; norwalk-like viruses; adenoviruses; astroviruses; sapporo-like viruses; toroviruses; coronaviruses; picornaviruses; herpes viruses; noroviruses; Candida; Aspergillus; *Candida albicans;* single-celled parasites; multi-celled parasites; ameobas; worms; tape worms; protozoans; flukes; roundworms; pinworms; hookworms; *Giradia lamblia*; cryptosporidium; and *Entamoeba histolytica.*

34. The system of any of claims 29-33, wherein the microbial cells are aerobic.

35. The system of any of claims 29-33, wherein the microbial cells are anaerobic.

36. The system of any of claims 29-35, wherein the system comprises both aerobic and anaerobic microbial cells.

37. The system of any of claims 29-36, wherein the microbial cells are present in the first cell culture channel.

38. The system of any of claims 29-37, wherein the system further comprises an anaerobic gas chamber in contact with at least part of the first cell culture channel.

39. The system of claim 38, wherein an oxygen gradient is established in the fluid flowing through the first cell culture channel.

40. The system of any of claims 1-39, wherein the membrane is at least partially porous.

41. The system of claim 40, wherein at least one pore aperture in the membrane is between 0.5 μm and 10 μm along a width dimension.

42. The system of any of claims 1-41, wherein the membrane comprises PDMS.

43. The system of any of claims 1-42, wherein the membrane is caused to stretch due to vacuum pressure.

44. The system of claim 43, wherein the system further comprises:

a first chamber wall of the device positioned adjacent to the at least one fluid channel, wherein the membrane is mounted to the first chamber wall;

a first operating channel adjacent to the at least one fluid channel on an opposing side of the first chamber wall, wherein a pressure differential applied between the first operating channel and the at least one fluid channel causes the first chamber wall to flex in a first desired direction to expand or contract along the plane defined by the membrane; and

a vacuum system providing a pressure differential between the at least one fluid channel the at least one operating channels, wherein the membrane stretches along the plane in response to the pressure differential.

45. The system of claim 44, further comprising;

a second chamber wall of the device positioned adjacent to the at least one fluid channel, wherein an opposing end of the membrane is mounted to the second chamber wall; and

a second operating channel positioned adjacent to the at least one fluid channel on an opposing side of the second chamber wall, wherein the pressure differential between to the second operating channel and the at least one fluid channel causes the second chamber wall to flex in a second desired direction to expand or contract along the plane defined by the membrane.

46. The system of any of claims 1-45, wherein the fluidics device comprises a microfluidic chip.

47. The system of any of claims 1-46, wherein the system is connected or coupled to a second cell culture system comprising cells or tissue which are not intestinal in origin.

48. The system of claim 47, wherein the second cell culture system comprises liver cells or tissue.

49. A method of producing an intestinal organoid comprising;

providing a fluid suitable for maintaining intestinal epithelial cells to the cell culture system of any of claims 1-48 such that the fluid contacts the intestinal epithelial cells; and

culturing the intestinal epithelial cells *in vitro*.

50. The method of claim 49, further comprising culturing the cells at least until villi structures are evident.

51. A system for evaluating intestinal effector agents comprising the cell culture system of any of Claims 1-48.

52. A method of evaluating intestinal treatments; comprising contacting the cells of the system of any of claim 1-48 with at least one candidate intestinal treatment effector; and

measuring the response of the cells in the system to determine the effect of the at least one candidate intestinal effector agent.

CLAIMS

1. A cell culture system comprising:

a fluidic device having a fluid channel connected to a fluid source, the fluid source supplying fluid to the fluid channel;

a membrane positioned within the channel between membrane support elements, at least portion of the membrane being flexible;

a membrane strain mechanism coupled to the membrane support elements capable of moving the membrane support elements and causing the membrane to stretch along at least one dimension of the membrane; and

at least one layer of intestinal epithelial cells comprising villi structures attached to at least one surface of the membrane;

in which the fluid flowing through the fluid channel is subject to an average shear stress of less than 1.0 dyne/cm^2.

2. A system according to Claim 1, in which the shear stress on the fluid flowing through the fluid channel is from 0.008 to 0.08 dyne/cm^2.

3. A system according to Claim 1 or 2, in which the shear stress on the fluid flowing through the fluid channel is approximately 0.018 dyne/cm^2.

4. A system according to Claim 1, 2 or 3, in which the shear stress on the fluid flowing through the fluid channel can vary over time.

5. A system according to Claim 4, in which the shear stress on the fluid flowing through the fluid channel can vary over time from 0 to 1000 dyne/cm^2.

6. A system according to Claim 4 or 5, in which the shear stress on the fluid flowing through the fluid channel can vary over time from 0.008 to 0.08 dyne/cm^2.

7. A system according to any preceding claim, in which the membrane is caused to stretch from 0% to 50%.

8. A system according to any of Claims 1 to 6, in which the membrane is caused to stretch from 5% to 15%.

9. A system according to any preceding claim, in which the membrane is caused to stretch approximately 10%.

10. A system according to any preceding claim, in which the membrane is caused to stretch more than 15% to create an abnormal condition/state of the intestinal epithelial cells; in which the abnormal condition/state models hypercontractility of the bowels.

11. A system according to any preceding claim, in which the membrane is caused to stretch in a cyclic manner at a rate in the range of 0.01 Hz to 2 Hz.

12. A system according to any preceding claim, in which the membrane is caused to stretch in a cyclic manner at a rate in the range of 0.05 Hz to 0.25 Hz.

13. A system according to any preceding claim, in which the membrane is caused to stretch in a cyclic manner at a rate of 0.15 Hz.

14. A system according to any of Claims 1 to 12, in which the membrane is caused to stretch in a cyclic manner at a rate greater than 0.2 Hz to create an abnormal condition/state of the intestinal epithelial cells; in which the abnormal condition/state models hypercontractility of the bowels..

15. A system according to any preceding claim, in which the membrane is caused to stretch in an irregular or intermittent manner.

16. A system according to any preceding claim, in which the fluid flows through the fluid channel at a flow rate less than 500 μL/hr.

17. A system according to any preceding claim, in which the fluid flows through the fluid channel at a flow rate less than 100 μL/hr.

18. A system according to any preceding claim, in which the fluid flows through the fluid channel at a flow rate from 0 to 50 μL/hr.

19. A system according to any preceding claim, in which the fluid flows through the fluid channel at a flow rate of approximately 30 μL/hr.

20. A system according to any preceding claim, further comprising at least one type of attachment molecule that supports adhesion of a plurality of living cells coating at least one side of the membrane.

21. A system according to Claim 20, in which the at least one attachment molecule is selected from the group consisting of:

collagen; collagen type I; MATRIGEL™; extracellular matrix; laminin; proteoglycan; vitronectin; fibronection; poly-D-lysine; polypeptides; oligonucleotides; DNA; and polysaccharide.

22. A system according to any preceding claim, in which the intestinal epithelial cells are mammalian or human cells.

23. A system according to any preceding claim, in which the intestinal epithelial cells are selected from the group consisting of:

Caco2 cells; HT-29 cells; primary small intestine epithelial cells; primary large intestine epithelial cells; iPS cells; ESC cells; stem cells; paneth cells; crypt cells; and mucus-secreting cells.

24. A system according to any preceding claim, in which the intestinal epithelial cells of the system further comprise villi structures.

25. A system according to any preceding claim, in which the system further comprises at least one layer of endothelial cells on at least the second surface of the membrane.

26. A system according to any preceding claim, in which the membrane is positioned such that it divides the fluid channel into a first cell culture channel and a second cell culture channel.

27. A system according to Claim 26, in which the first cell culture channel comprises intestinal epithelial cells.

28. A system according to Claim 26 or 27, in which the second cell culture channel comprises cells selected from the group consisting of:

endothelial cells, immune cells, and connective tissue cells.

29. A system according to any of Claims 1 to 27, in which the system further comprises microbial cells or pathogens.

30. A system according to Claim 29, in which the microbial cells are maintained in the system for at least 1 day.

31. A system according to Claim 29 or 30, in which the microbial cells are selected from the group consisting of:

Lactobacillus; Bacterioides; Ruminococcus; Peptococcus; Peptostreptococcus; Bifidobacterium; Escherichia; Achromobacter; *Acidaminococcus fermentans; Acinetobacter cacoaceticus*; Aeromonas; *Alcaligenes faecalis*; Bacillus; *Butyriviberio fibrosolvens*; Camplyobacter; *Campylobacter coli; Clostridium difficile; Clostridium sordelli*; *Enterobacter cloacae; Enterococcus faecalis; Enterococcus faecium; Escherichia coli*; Flavobacterium; Mycobacterium; Mycoplasma; *Plesiomonas shigelloides*; *Propionibacterium acnes*; *Pseudomonas aeruginosa*; *Ruminococcus bromii*; Sarcina; *Staphylococcus aureus*; *Streptococcus anginosus;* Veillonella; Vibrio; *Yersinia enterocolitica; Lactobacillus rhamnosus; Lactobacillus rhamnosus* GG; *Bifidobacterium breve; Bifidobacterium longum; Bifidobacterium infantis; Lactobacillus acidophilus; Lactobacillus plantarum; Lactobacillus paracasei; Lactobacillus bulgaricus*; and *Streptococcus thermophilus*.

32. A system according to Claim 29 or 30, in which the microbial cells are pathogenic.

33. A system according to Claim 29 or 32, in which the pathogens are selected from the group consisting of:

enterotoxigenic *Escherichia coli*; *Bilophila wadsworthia;* Shigella; Yersinia; Pleisiomonas; Vibrio; Aeromonas; Campylobacter; Crytosporidia; Coccidosis; Salmonella; *Helicobacter pylori*; *Clostridium difficile*; *Salmonella kedougou*; Bacteroides; Clostridium; Firmicutes; *Shigellia dysenteriae*; *Salmonella enterica*; *Salmonella typhi;* Listeria; *Listeria monocytogenes; Vibrio parahaemolyticus*; Proteus; *Vibrio cholerae; Enterococcus faecalis; Yersinia enterocolitica;* and *Campylobacter jejuni;* rotavirus; norwalk-like viruses; adenoviruses; astroviruses; sapporo-like viruses; toroviruses; coronaviruses; picornaviruses; herpes viruses; noroviruses; Candida; Aspergillus; *Candida albicans;* single-celled parasites; multi-celled parasites; ameobas; worms; tape worms; protozoans; flukes; roundworms; pinworms; hookworms; *Giradia lamblia*; cryptosporidium; and *Entamoeba histolytica*.

34. A system according to any of Claims 29 to 33, in which the microbial cells are aerobic.

35. A system according to any of Claims 29 to 33, in which the microbial cells are anaerobic.

36. A system according to any of Claims 29 to 35, in which the system comprises both aerobic and anaerobic microbial cells.

37. A system according to any of Claims 29 to 36, in which the microbial cells are present in the first cell culture channel.

38. A system according to any of Claims 29 to 37, in which the system further comprises an anaerobic gas chamber in contact with at least part of the first cell culture channel.

39. A system according to Claim 38, in which an oxygen gradient is established in the fluid flowing through the first cell culture channel.

40. A system according to any preceding claim, in which the membrane is at least partially porous.

41. A system according to Claim 40, in which at least one pore aperture in the membrane is between 0.5 μm and 10 μm along a width dimension.

42. A system according to any preceding claim, in which the membrane comprises PDMS.

43. A system according to any preceding claim, in which the membrane is caused to stretch due to vacuum pressure.

44. A system according to Claim 43, in which the system further comprises:

a first chamber wall of the device positioned adjacent to the at least one fluid channel, in which the membrane is mounted to the first chamber wall;

a first operating channel adjacent to the at least one fluid channel on an opposing side of the first chamber wall, in which a pressure differential applied between the first operating channel and the at least one fluid channel causes the first chamber wall to flex in a first desired direction to expand or contract along the plane defined by the membrane; and

a vacuum system providing a pressure differential between the at least one fluid channel the at least one operating channels, in which the membrane stretches along the plane in response to the pressure differential.

45. A system according to Claim 44, further comprising;

a second chamber wall of the device positioned adjacent to the at least one fluid channel, in which an opposing end of the membrane is mounted to the second chamber wall; and

a second operating channel positioned adjacent to the at least one fluid channel on an opposing side of the second chamber wall, in which the pressure differential between to the second operating channel and the at least one fluid channel causes the second chamber wall to flex in a second desired direction to expand or contract along the plane defined by the membrane.

46. A system according to any preceding claim, in which the fluidics device comprises a microfluidic chip.

47. A system according to any preceding claim, in which the system is connected or coupled to a second cell culture system comprising cells or tissue which are not intestinal in origin.

48. A system according to Claim 47, in which the second cell culture system comprises liver cells or tissue.

49. A method of producing an intestinal organoid comprising;

providing a fluid suitable for maintaining intestinal epithelial cells to the cell culture system of any preceding claim such that the fluid contacts the intestinal epithelial cells; and

culturing the intestinal epithelial cells *in vitro*.

50. A method according to Claim 49, further comprising culturing the cells at least until villi structures are evident.

51. A system for evaluating intestinal effector agents comprising a cell culture system according to any of Claims 1 to 48.

52. A method of evaluating intestinal treatments; comprising contacting the cells of a system according to any of Claims 1 to 48 with at least one candidate intestinal treatment effector; and

measuring the response of the cells in the system to determine the effect of the at least one candidate intestinal effector agent.