Claims

What is claimed is:

1. A method of selecting an immune checkpoint inhibitor *in vivo*, comprising (a) *in vitro* co-culturing adherent tumor cells and suspension immune cells within lumens of microtube array membrane (MTAM), wherein the MTAM comprises electrospun fiber assembly having highly aligned and closely packed hollow fibers with nano-size; (b) transplanting the membrane into a non-human animal; and (c) administering an immune checkpoint inhibitor to the non-human animal; (d) separating the tumor cells and the immune cells; and (e) determining a cell viability of the tumor cells or the activity of the immune cells or determining immune checkpoint protein expression in the tumor or immune cells; wherein the immune checkpoint inhibitor has an anti-tumor effect if the cell viability of the tumor cells is significantly lower than that of the control or the activity of the immune cells is significantly higher than that of the control; or if the immune checkpoint protein expression in the tumor or immune cells is changed relative to the control.

2. The method of Claim 1, wherein the adherent tumor cells or the suspension immune cells are seeded at a concentration of about 1×10^4 cells/μl to 1×10^7 cells/μl.

3. The method of Claim 1, wherein the adherent tumor cells are cells of hepatocellular carcinoma, colorectal carcinoma, glioblastoma, gastric cancer, esophageal cancer, non-small cell lung cancer (NSCLC), pancreatic cancer, renal cell carcinoma, benign prostate hyperplasia, prostate cancer, ovarian cancer, melanoma, breast cancer, chronic lymphocytic leukemia (CLL), Merkel cell carcinoma, small cell lung cancer (SCLC), Non-Hodgkin lymphoma, acute myeloid leukemia (AML), gallbladder cancer and cholangiocarcinoma, urinary bladder cancer, or uterine cancer.

~~4. The method of Claim 1, wherein the suspension immune cells include, but are not limited to, peripheral blood mononuclear cells (PBMCs), lymphocytes, T lymphocytes (such as CD8-positive T lymphocytes), T cells such as CD4-positive T-cell, CD8-positive T cells, CD4-positive helper T cells, CD4-positive-helper-T cells and CD8-positive cytotoxic T cells), T helper cells, monocytes, natural killer (NK) cells, macrophages, or granulocytes.~~

~~5. The method of Claim 1, wherein the non-human animal is a rodent (such as murine), a rabbit, a dog, a pig or a monkey. In some embodiments, the non-human animal is a murine such as rat and mice.~~

~~6. The method of Claim 1, wherein the immune checkpoint inhibitor inhibits the PD1 pathway or the CTLA4 pathway.~~

~~7. The method of Claim 6, wherein the immune checkpoint inhibitor is an antibody (e.g., a monoclonal antibody, chimeric antibody, humanized antibody and human antibody), an engineered binding protein, a soluble receptor, an aptamer, a peptide, or a small molecule that binds to an immune checkpoint protein.~~

~~8. The method of Claim 1, wherein the immune checkpoint inhibitor binds to PD1, PD-L1, PD-L2 or CTLA4.~~

~~9. The method of Claim 1, wherein he *in vitro* co-culturing of step (a) takes about 1 to about 2 days.~~

~~10. The method of Claim 1, wherein the administration of an immune checkpoint inhibitor in step (c) is conducted after about 1 to about 3 days of the transplantation of step (b).~~

~~11. The method of Claim 1, wherein the cell viability of tumor cells or the activity of immune cells or the immune checkpoint protein expression is determined after about 8 to about 15 days of the administration of step (c).~~

~~12. The method of Claim 1, wherein the total time from step (b) to step (d) takes about 9 days to 18 days.~~

~~13. The method of Claim 1, wherein the total time from step (b) to step (d) takes about 10 days.~~

~~14. The method of Claim 1, wherein the *in vitro* co-culturing of step (a) takes about 1 to about 2 days.~~

~~15. The method of Claim 1, wherein the MTAM comprises one or more layers of a highly aligned and closely packed electrospun fiber assembly, wherein at least five (5) electrospun fibers are packed together to form a single layer and an orientation of the electro spun fibers is no greater than +/−5° relative to a longitudinal axis of the assembly, wherein the electrospun fibers are connected so that the electrospun fibers are aligned and closely packed to form the single layer, and wherein the alignment of the fibers is in the orientation no greater than +/−5°.~~

~~16. The method of Claim 1, wherein the MTAM has one or more layers of hollow electrospinning fiber assembly, wherein the fibers have nanoscale hair like structures extended from inner surface thereof.~~

~~17. The method of Claim 1, which comprises at least two layers of the fiber assembly.~~

~~18. The method of Claim 17, which has a structure wherein the layers of fibers are alternatively or perpendicularly arranged.~~

~~19. The method of Claim 1, wherein the MTAM is enclosed in a pocket.~~

~~20~~1. A method of selecting an immune checkpoint inhibitor *in vitro*, comprising (a) *in vitro* co-culturing adherent tumor cells and suspension immune cells within lumens of ~~porous hollow fibers membrane of the invention~~ a microtube array membrane; (b) adding an immune checkpoint inhibitor to the ~~membrane~~ lumens of the microtube array membrane; (c) separating the adherent

tumor cells and the suspension immune cells by centrifugation and determining a cell viability of the adherent tumor cells or the activity of the suspension immune cells ~~or determining immune checkpoint protein expression in the tumor or immune cells~~; wherein the immune checkpoint inhibitor has an anti-tumor effect if the cell viability of the adherent tumor cells is significantly lower than that of ~~the~~ a control or the activity of the suspension immune cells is significantly higher than that of the control~~; or if the immune checkpoint protein expression in the tumor or immune cells is changed relative to the control~~.

2. The method of Claim 1, wherein the adherent tumor cells or the suspension immune cells are seeded at a concentration of 1 x 10^4 cells/μl to 1 x 10^7 cells/μl.

3. The method of Claim 1, wherein the adherent tumor cells are cells of hepatocellular carcinoma, colorectal carcinoma, glioblastoma, gastric cancer, esophageal cancer, non-small cell lung cancer, pancreatic cancer, renal cell carcinoma, benign prostate hyperplasia, prostate cancer, ovarian cancer, melanoma, breast cancer, chronic lymphocytic leukemia, Merkel cell carcinoma, small cell lung cancer, Non-Hodgkin lymphoma, acute myeloid leukemia, gallbladder cancer and cholangiocarcinoma, urinary bladder cancer, or uterine cancer.

4. The method of Claim 1, wherein the suspension immune cells include peripheral blood mononuclear cells, lymphocytes, monocytes, macrophages, or granulocytes.

5. The method of Claim 4, wherein the suspension immune cells comprise T cells or natural killer (NK) cells.

6. The method of Claim 5, wherein the suspension immune cells comprise T helper cells.

7. The method of Claim 5, wherein the suspension immune cells comprise CD4-positive T-cell, CD8-positive T cells, CD4-positive helper T cells, CD4-positive-helper-T cells or CD8-positive cytotoxic T cells.

8. The method of Claim 1, wherein the immune checkpoint inhibitor inhibits the PD1 pathway or the CTLA4 pathway.

9. The method of Claim 8, wherein the immune checkpoint inhibitor is an antibody, an engineered binding protein, a soluble receptor, an aptamer, a peptide, or a small molecule that binds to an immune checkpoint protein.

10. The method of Claim 1, wherein the immune checkpoint inhibitor binds to PD1, PD-L1, PD-L2 or CTLA4.

11. The method of Claim 1, wherein the *in vitro* co-culturing of step (a) takes 1 to 2 days.

12. The method of Claim 1, wherein the microtube array membrane comprises one or more layers of a highly aligned and closely packed electrospun fiber assembly, wherein at least five (5) electrospun fibers are packed together to form a single layer and an orientation of the electro spun fibers is no greater than +/−5° relative to a longitudinal axis of the assembly, wherein the electrospun fibers are connected so that the electrospun fibers are aligned and closely packed to form the single layer, and wherein the alignment of the fibers is in the orientation no greater than +/−5°.

13. The method of Claim 1, wherein the microtube array membrane has one or more layers of hollow electrospinning fiber assembly, wherein the fibers have nanoscale hair like structures extended from inner surface thereof.

14. The method of Claim 1, wherein the microtube array membrane comprises at least two layers of the fiber assembly.

15. The method of Claim 14, wherein the microtube array membrane has a structure wherein the layers of fibers are alternatively or perpendicularly arranged.