CLAIMS

1. A method of preparing an augmented NeuroImmunotherapeutic immune cell, the method comprising:

a. providing a first immune cell;

b. contacting said first immune cell with at least one molecule selected from a neurotransmitter or analog thereof, a neuropeptide or analog thereof, and a modulator of a voltage gated ion channel;

c. measuring at least one of:

i. Programmed Cell Death 1 (PD-1) expression level or functional level in said first immune cell;

ii. proliferation of said first immune cell alone in culture;

iii. proliferation of said first immune cell in coculture with a cancerous cell; and

iv. cell death of cancerous cells in coculture with said first immune cell;

d. providing a second immune cell whose origin is the same as said first immune cell;

e. contacting said second immune cell with said at least one molecule wherein said at least one molecule decreased PD-1 expression or function in said first immune cell, increased proliferation of said first immune cell alone or in coculture, increased cancerous cell death in coculture with said first immune cell or a combination thereof to obtain the augmented NeuroImmunotherapeutic immune cell.

2. The method of claim 1, wherein

said first and second immune cells are immune cells that expresses PD-1;

said first and second immune cells is a T cell;

said first and second immune cells are from a subject that is to be administered the augmented NeuroImmunotherapeutic immune cell, or said first and second immune cells are from a healthy donor;

said first immune cell is not pre-activated before said contacting; or

any combination thereof.

3. The method of claim 1 or 2, wherein said first provided immune cell is multiple immune cells and the method further comprising selecting from said first provided immune cells a subset of immune cells.

4. The method of claim 3, wherein said subset of immune cells is selected from the group consisting: effector T cells, helper T cells, cytotoxic T cells, regulator T cells, suppressor T cells, natural killer T cell, inflammatory T cells, memory T cells, gamma delta T cells, tissue/organ-infiltrating T cells, tumor-infiltrating T cells, repairing T cells and pro-regenerative T cells, mucosal associated T cells, repairing T cells, pro-regenerative T cells, activated T cells, and inactivated T cells.

5. The method of any one of claims 1 to 4, further comprising:

culturing said immune cells in immune cell media comprising human plasma or serum,;

expanding said immune cells; or

a combination thereof

wherein said expanding comprises stimulation of said immune cells;

wherein said culturing is for a period of time sufficient to bring at least 50% of said provided immune cells to a resting state, wherein said culturing is for between 1 and 7 days, and wherein said stimulation comprises incubating said immune cell with at least one of CD3, CD28, mitogen, a growth factor and a cytokine.

6. The method of claim 1 or 2, wherein

said first immune cell is multiple immune cells, and said first immune cells are divided and cultured separately and contacted with said at least one molecule, and said at least one molecule which effects the largest increase in proliferation of said first immune cell alone or in coculture, or largest increase in cancerous cell death in coculture or the largest decrease in PD-1 expression or function in said first immune cell, is selected; or

said second immune cell is multiple immune cells, and said second immune cells are divided and contacted with said at least one molecule sequentially.

7. The method of any one of claims 1 to 6, wherein:

(a) said neurotransmitter or analog thereof is selected from: dopamine, glutamate, a dopamine receptor agonist, a glutamate/AMPA/NMDA receptor agonist, a glutamate/AMPA/NMDA receptor antagonist, and a dopamine receptor antagonist;

(b) said neuropeptide or analog thereof is selected from GnRH-I, GnRH-II, Calcitonin gene-related peptide (CGRP), Somatostatin, Neuropeptide Y (NPY), GnRH-I receptor agonist, GnRH-I receptor antagonist, GnRH-II receptor agonist, GnRH-II receptor antagonist, CGRP receptor agonist, CGRP receptor antagonist, Somatostatin receptor agonist, Somatostatin receptor antagonist, NPY receptor agonist, and NPY receptor antagonist; and

(c) said modulator of a voltage gated ion channel is selected from the group consisting of a modulator of a voltage-gated sodium channel, calcium channel, potassium channel (Kv) and chloride channel.

8. The method of claim 7, wherein

(a) said dopamine receptor agonist is selected from:

(1) a dopamine D1/5 receptor agonist selected from dopamine, fenoldopam, corlopam, A77636, and SKF38393;

(2) a dopamine D2 receptor agonist, wherein said dopamine D2 receptor agonist is sumanirole;

(3) a dopamine D3 receptor agonist selected from PD 128907 and 7-OH-DPAT; and

(4) a dopamine D4 receptor agonist selected from PD 168077 and A412997;

(b) said dopamine receptor antagonist is selected from:

(1) a dopamine D1/5 receptor antagonist, wherein said a dopamine D1/5 receptor antagonist is SCH 39166;

(2) a dopamine D2 receptor antagonist, wherein said dopamine D2 receptor antagonist is L-741626;

(3) a dopamine D3 receptor antagonist, wherein said dopamine D3 receptor antagonist is NGB 2904; and

(4) a dopamine D4 receptor antagonist, wherein said dopamine D4 receptor antagonist is L-741742;

(c) said glutamate/AMPA/NMDA receptor agonist is selected from glutamate, AMPA, and NMDA;

(d) said glutamate/AMPA/NMDA receptor antagonist is selected from CNQX and MK801; and

(e) said voltage gated potassium channel is Kv1.1, and wherein said modulator of a voltage gated ion channel is a voltage-gated Kv1.1 ion channel blocker selected from dendrotoxin K (DTX-K) and an anti-Kv1.1 blocking antibody.

9. The method of any one of claims 1 to 8, wherein said first immune cell has been frozen in freezing media comprising human plasma or serum, and thawed before contacting said first immune cell with said at least one molecule.

10. A method of selecting a subject suitable for NeuroImmunotherapy, the method comprising,

a. providing an immune cell from said subject;

b. contacting said immune cell with at least one molecule selected from a neurotransmitter or analog thereof, a neuropeptide or analog thereof, and a modulator of a voltage gated ion channel;

c. measuring at least one of:

i. programmed cell death 1 (PD-1) expression on said immune cell;

ii. proliferation of said immune cell alone in culture;

iii. proliferation of said immune cell in coculture with a cancerous cell; and

iv. cell death of cancerous cells in coculture with said immune cell;

wherein at least one of a decrease in PD-1 expression or function, an increase in proliferation of said immune cell alone or in coculture, an increase in cancerous cell death and a combination thereof indicates said subject is suitable for NeuroImmunotherapy.

11. A method of selecting a combination of molecules for improving therapeutic immune cell potential, the method comprising:

a. providing an immune cell;

b. contacting said first immune cell with at least two molecules selected from a neurotransmitter or analog thereof, and a neuropeptide or analog thereof, or a modulator of a voltage gated ion channel;

c. measuring at least one of:

i. PD-1 expression or activity on said immune cell;
ii. proliferation of said immune cell in coculture with a cancerous cell; and
iii. cell death of cancerous cells in coculture with said immune cell;
iv. proliferation of said immune cell alone in culture;
v. expression of CD3 zeta-chain in said immune cell;
vi. migration of said immune cells
vii. adhesion of said immune cells;
viii. homing of said immune cells;
ix. penetration of said immune cells
x. secretion of cytokines by said immune cells;
xi. secretion of therapeutic proteins by said immune cells; and
xii. expression levels and functional levels of proteins and genes involved in processes i to xi;

wherein at least one of a decrease in PD-1 expression or activity, an increase in proliferation of the immune cell alone or in coculture, an increase in cancerous cell death, an increase in zeta-chain expression, an increase in migration, an increase in cytokine secretion, an increase in adhesion, an increase in homing, an increase in secretion of at least one therapeutic protein, a decrease in expression or function of at least one protein or gene involved in the process of i, or an increase in expression or function of at least one protein or gene involved in the processes of ii to xi indicates said at least two molecules improve therapeutic potential of said immune cell, wherein said immune cell's immunotherapy potential is said cell's potential for treating a disease, condition, wound or injury in which there is or is suspected to be suboptimal T cell number, activity or both.

12. A method of decreasing PD-1 expression in a cell, the method comprising contacting the cell with at least one molecule selected from a neurotransmitter or analog thereof, a neuropeptide or analog thereof, or a modulator of a voltage gated ion channel.

13. A method of augmenting immune cell function, the method comprising:

a. providing an immune cell; and

b. contacting said immune cell with at least two molecules selected from a neurotransmitter or analog thereof, a neuropeptide or analog thereof, and a modulator of a voltage gated ion channel.

14. The method of any one of claims 10 to 13, wherein:

(a) said neurotransmitter or analog thereof is selected from: dopamine, glutamate, a dopamine receptor agonist, a glutamate/AMPA/NMDA receptor agonist, a glutamate/AMPA/NMDA receptor antagonist, and a dopamine receptor antagonist;

(b) said neuropeptide or analog thereof is selected from GnRH-I, GnRH-II, CGRP, somatostatin, Neuropeptide Y (NPY), GnRH-I receptor agonist, GnRH-I receptor antagonist, GnRH-II receptor agonist, GnRH-II receptor antagonist, CGRP receptor agonist, CGRP receptor antagonist, Somatostatin receptor agonist, Somatostatin receptor antagonist, NPY receptor agonist, and NPY receptor antagonist; and

(c) said modulator of a voltage gated ion channel is selected from the group consisting of a modulator of a voltage-gated sodium channel, calcium channel, potassium channel (Kv) and chloride channel.

15. Use of an augmented NeuroImmunotherapeutic immune cell prepared by the method of any one of claims 1 to 9 in the manufacture of a medicament for the treatment of a disease, condition, injury or wound in a subject that has, or is suspected to have, suboptimal T cell number, activity or both,

wherein said disease, condition, injury or wound is selected from the group consisting of: a cancer, an infectious disease, a genetic immunodeficiency, an acquired immunodeficiency, a degenerative disease, autoimmune disease, metabolic disease, genetic disease, a neurological or neuropsychiatric disease, and post-organ transplant accompanied by immune incompetence.

16. The use of claim 15, wherein the medicament is a subset of said augmented NeuroImmunotherapeutic immune cell.

17. The use of claim 15 or 16, wherein the medicament comprises between 2 x 10^6 and 10^9 of said augmented NeuroImmunotherapeutic immune cell.

18. The use of any one of claims 15 to 17, wherein the medicament is to be administered to the subject repeatedly.

19. The use of any one of claims 15 to 17, wherein the medicament is to be administered to the subject indefinitely.

20. The use of any one of claims 15 to 19, wherein the medicament performs at least one of the following functions in the subject:

a. kill disease-causing cells;
b. kill an infectious organism;
c. cure said disease or condition;
d. repair a tissue or organ;
e. replace damaged cells, or tissue;
f. compensate for a loss or deficiency;
g. prevent said disease or condition; and
h. regenerate a tissue or organ.