pluripotent stem cells (hiPSCs), which may be obtained from patient or carrier cell samples, *e.g.* adipocytes, keratinocytes, fibroblasts, and the like. The hiPSCs are induced to develop an ectoderm fate *in vitro* and subsequently differentiated into spheroids that contain oligodendrocytes- human oligodendro-spheroids (hOS), as well as neural progenitors, astrocytes and neurons. The cell populations can be isolated from the hOS, or the intact hOS can be used as a model for interacting cell populations. The hOS and cells derived therefrom may be used for transplantation, for experimental evaluation, as a source of lineage and cell specific products, and the like. In some examples the cell cultures are feeder-free and xeno-free.

[0009a] In a first aspect, the present disclosure refers to a method for producing human oligodendrocytes in vitro, the method comprising: (i) inducing in an induced pluripotent stem cell suspension culture a neural fate by culturing intact colonies or aggregates of single cells of the pluripotent stem cells for a period of from 2 to 10 days in medium comprising an effective dose of an inhibitor of BMP and an inhibitor of TGFβ to produce a population of floating spheroids; (ii) culturing the floating spheroids for a period of 1 week to 4 weeks in neural media supplemented with an effective dose of FGF2 and EGF to provide a spheroid of neural progenitor cells; (iii) differentiating the spheroid of neural progenitor cells to a human oligodendro-spheroid (hOS) comprising oligodendrocytes by culturing the spheroid of neural progenitor cells in neural medium lacking FGF2 and EGF, and comprising an effective dose of PDGF-AA, IGF-1, HGF, BDNF, NT3, insulin, cAMP, T3 and biotin; and (iv) maintaining the hOS for at least 1 month in neural medium in the absence of growth factors to derive cultures that include myelinating oligodendrocytes, neurons and astrocytes.

[0010] In some examples of the disclosure, populations of purified human OPC or oligodendrocytes are provided, including without limitation disease-relevant oligodendrocytes, where the cells are differentiated from induced human pluripotent stem cells (hiPSCs). In some examples a panel of such *in vitro* derived cells are provided, where the panel includes two or more genetically different cells. In some examples a panel of such cells are provided, where the cells can be subjected to a plurality of candidate agents, or a plurality of doses of a candidate agent. Candidate agents include small molecules, i.e. drugs, genetic constructs that increase or decrease expression of an RNA of interest, electrical changes, and the like. In some examples a panel refers to a system or method utilizing patient-specific cells from two or more distinct conditions, and may be three or more, four or more, five or more, six or more, seven or more genetically distinct conditions.

[0011] In some examples of the disclosure, methods are provided for determining the activity of a candidate agent on oligodendrocytes from the hOS, the method comprising contacting the candidate agent with one or a panel of purified neurons, astrocytes, OPSs or oligodendrocyte populations differentiated from induced human pluripotent stem cells (hiPSCs). The cell populations optionally comprise at least one allele encoding a mutation associated or causing a myelinating or demyelinating disease or an oligodendrocyte development disorder; and determining the effect of the agent on morphologic, genetic or functional parameters, including without limitation gene expression profiling. In a second aspect, the present disclosure refers to a method of determining the effect of a candidate agent on human oligodendrocytes, the method comprising: producing one or a panel of oligodendrocytes differentiated from induced human pluripotent stem cells (hiPSC) according to the method disclosed herein, contacting the candidate agent with one or a panel of oligodendrocytes differentiated from induced human pluripotent stem cells (hiPSC), wherein the oligodendrocytes optionally comprise at least one allele encoding a mutation associated with a neural disease; and determining the effect of the agent on morphologic, genetic or functional parameters. The screening methods may be combined with immune effector cells to determine activity of such immune cells of oligodendrocytes and myelination, or the interaction between oligodendrocytes, astrocytes in hOS and autologous immune cells from patients. Methods of analysis at the single cell level are of particular interest, e.g. myelination assays, single cell gene expression, effect of oligodendrocytes on neurons or astrocytes, and neuronal cell signal transmission, and the like. Candidate agents include immune effector cells, e.g. T cells, microglial cells, macrophages, NK cells, etc., and immune

THAT WHICH IS CLAIMED IS:

1. A method for producing human oligodendrocytes in vitro, the method comprising:

(i) inducing in an induced pluripotent stem cell suspension culture a neural fate by culturing intact colonies or aggregates of single cells of the pluripotent stem cells for a period of from 2 to 10 days in medium comprising an effective dose of an inhibitor of BMP and an inhibitor of TGFβ to produce a population of floating spheroids;

(ii) culturing the floating spheroids for a period of 1 week to 4 weeks in neural media supplemented with an effective dose of FGF2 and EGF to provide a spheroid of neural progenitor cells;

(iii) differentiating the spheroid of neural progenitor cells to a human oligodendro-spheroid (hOS) comprising oligodendrocytes by culturing the spheroid of neural progenitor cells in neural medium lacking FGF2 and EGF, and comprising an effective dose of PDGF-AA, IGF-1, HGF, BDNF, NT3, insulin, cAMP, T3 and biotin; and

(iv) maintaining the hOS for at least 1 month in neural medium in the absence of growth factors to derive cultures that include myelinating oligodendrocytes, neurons and astrocytes.

2. The method of Claim 1, wherein the cells comprise at least one mutated allele associated with a myelin disorder.

3. The method of claim 1 or claim 2, wherein the medium in step (i) comprises a dose of dorsomorphin and SB-431542 effective to induce pluripotent stem cells to a neural fate.

4. The method of Claim 3, wherein the suspension culture of step (i) is feeder layer free.

5. The method of Claim 4, wherein the medium of step (i) further comprises an effective dose of an inhibitor of wnt.

6. The method of Claim 5, further comprising the spheroid of step (ii) with sonic hedgehog pathway agonists and retinoic acid or with sonic hedgehog pathway agonists and Wnt inhibitors.

7. The method of Claim 6, wherein the neural medium of step (iii) further comprises insulin, cAMP, T3, and biotin.

8. The method of Claim 7, wherein the neural medium in step (iv) comprises ascorbic acid, insulin, cAMP, T3, and biotin.

9. The method of Claim 8, further comprising isolating oligodendrocytes from a human oligodendro-spheroid by flow cytometry, magnetic immunoselection, or immunopanning.

10. The method of Claim 9, wherein the oligodendrocytes are combined with neurons or neuronal progenitor cells.

11. A method of determining the effect of a candidate agent on human oligodendrocytes, the method comprising:

producing one or a panel of oligodendrocytes differentiated from induced human pluripotent stem cells (hiPSC) according to the method of Claim 9,

contacting the candidate agent with one or a panel of oligodendrocytes differentiated from induced human pluripotent stem cells (hiPSC),

wherein the oligodendrocytes optionally comprise at least one allele encoding a mutation associated with a neural disease; and

determining the effect of the agent on morphologic, genetic or functional parameters.

12. The method of claim 11 wherein the candidate agent is an immune effector cell or an immune modulatory agent.

13. The method of Claim 11, wherein a panel of human oligodendrocytes comprises at least two oligodendrocytes having differing genotypes.

14. The method of Claim 13, wherein a panel of human oligodendrocytes comprises oligodendrocytes cultured under differing environmental conditions.