【CLAIMS】

【Claim 1】

A composition for direct reprogramming urine cells into neural stem cells, the composition comprising:

(i) an Oct4 protein or a nucleic acid encoding the Oct4 protein;

(ii) a Sox2 protein or a nucleic acid encoding the Sox2 protein;

(iii) a Klf4 protein or a nucleic acid encoding the Klf4 protein; ~~and~~

(iv) a Glis1 protein or a nucleic acid encoding the Glis1 protein; and

(v) culture medium obtained by mixing a DMEM/F12 medium and a neurobasal medium at a volume ratio of 1 : 1, wherein the culture medium comprises N2, B27, human LIF, SB431542, and CHIR99021.

【Claim 2】

The composition of claim 1, wherein the urine cells are somatic cells derived from urine.

【Claim 3】

The composition of claim 1, wherein the nucleic acids encoding the Oct4, Sox2, Klf4, and Glis1 proteins are synthetic mRNA.

【Claim 4】

A method for direct reprogramming of urine cells into neural stem cells, the method comprising:

(a) isolating urine cells from urine and culturing the urine cells;

(b) introducing the composition of claim 1 or 3 into the cultured urine cells;

(c) inducing direct reprogramming into neural stem cells by culturing urine cells into which the composition has been introduced in a neural stem cell-inducing medium; and

(d) selecting a neural stem cell line having characteristics similar to neural stem cell from the cells in which direct reprogramming has been induced by the

neural stem cell-inducing medium,

wherein in step (c), the culture medium is obtained by mixing a DMEM/F12 medium and a neurobasal medium at a volume ratio of 1 : 1 and adding N2, B27, human LIF, SB431542, and CHIR99021 to the medium mixture.

【Claim 5】

The method of claim 4, wherein in step (b), the introduction of synthetic mRNA encoding the Oct4, Sox2, Klf4, and Glis1 is introducing the synthetic mRNA using electroporation.

~~【Claim 6】~~

~~The method of claim 4, wherein in step (c), the culture medium is obtained by mixing a DMEM/F12 medium and a neurobasal medium at a volume ratio of 1 : 1 and adding 1xN2, 1xB27, human LIF, a TGF-beta inhibitor, and a GSK3 beta inhibitor to the medium mixture.~~

【Claim ~~7~~6】

The method of claim ~~6~~4, wherein the culture medium further comprises one or more of ~~a Shh agonist, an adenylyl cyclase activator, a histone deacetylase inhibitor~~ purmorphamine, forskolin, sodium butyrate, and ascorbic acid 2-phosphate.

【Claim ~~8~~7】

The method of claim ~~7~~6, wherein the culture in the culture medium is performed under low oxygen (O_2 hypoxia) conditions.

【Claim ~~9~~8】

A pharmaceutical composition for the prevention or treatment of neurological damage diseases comprising the directly reprogrammed neural stem cells expressing OTX2 and HOXB2 prepared by the method of any one of claims 4 to ~~8~~ 7 as an active ingredient.

【Claim ~~10~~9】

The pharmaceutical composition of claim ~~9~~8, wherein the neurological damage disease is selected from the group consisting of Parkinson's disease, Alzheimer's

disease, Pick's disease, Huntington's disease, amyotrophic lateral sclerosis, an ischemic brain disease (stroke), a demyelinating disease, multiple sclerosis, epilepsy, a degenerative neurological disease, and spinal cord injury.

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