International Standard

ISO 18162

Biotechnology — Biobanking — Requirements for human neural stem cells derived from pluripotent stem cells

Biotechnologie — Biobanque — Exigences relatives aux cellules souches neuronales humaines dérivées de cellules souches pluripotentes

First edition
2024-12

Reference number
ISO 18162:2024(en)

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Published in Switzerland

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Foreword

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This document was prepared by ISO/TC 276, *Biotechnology*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Neural stem cells (NSCs) are the adult stem cells in the central nervous system (CNS). NSCs have self-renewal ability and multipotency. NSCs can differentiate into various neurons and glial cells including astrocytes and oligodendrocytes. NSCs play a major role in embryonic development and adult neurogenesis. According to the hypothesis by Alvarez-Buylla, there are several types of cells can be called NSCs, including neuroepithelium – epithelial cells of the ventricular zone (VZ) of the neural tube[1], radial glial cells (RGCs) and basal (intermediate) progenitor cell (IPC)[2-4]. In the adult, NSCs are restricted to specific brain regions, such as the subventricular zone (SVZ) of the lateral ventricles and the subgranular zone (SGZ) of the dentate gyrus (DG) of the hippocampus[5].

NOTE The term "neural" refers to any type of nerve cell, including a mixture of brain cells, whereas "neuronal" is specifically related to neurons.

Despite these advances, substantial ambiguities persist regarding the nomenclature, nature, identity, function, mode of isolation and experimental handling of these cells. NSCs are not fully defined by the initial minimal criteria proposed out, and as such require careful characterization by a matrix of functional assays.

NSCs have been isolated from human fetal CNS (brain or spinal cord), cerebrospinal fluid, biopsy and autopsy material, or differentiated from pluripotent stem cells (PSCs), which are widely used for animal and clinical research[6]. NSCs generated from different sources or differentiation protocols have different properties. Different institutions use different practices for isolating, processing and biobanking these NSCs, making it difficult to compare data and results across institutions. Thus, there is a need for standardized approaches to isolate, process, expand and cryopreserve these NSCs.

The aim of this document is to provide general guidance for biobanking of human NSCs derived from pluripotent stem cells (hPSC-NSCs) for research purposes. This document is applicable for academic centers, public and private institutions performing a biobanking service of hPSC-NSCs for R&D (Research and Development) and preclinical studies, not for clinical use.

Importantly, this document is focused on hPSC-NSCs that have been isolated, manipulated and/or propagated from hPSCs in culture for research purposes.

Biotechnology — Biobanking — Requirements for human neural stem cells derived from pluripotent stem cells

1 Scope

This document specifies requirements for the biobanking of human neural stem cells (hPSC-NSCs) derived from human pluripotent stem cells (hPSCs), including the requirements for the differentiaton, culture, characterization, quality control (QC), storage, thawing and transport of hPSC-NSCs.

Requirements for the collection of biological source material, the transport to and reception of biological source material and hPSCs at the biobank, as well as the establishment, expansion and QC of hPSCs are covered in ISO 24603.

This document is applicable to all organizations performing biobanking of hPSC-NSCs used for research and development in the life sciences.

This document does not apply to hPSC-NSCs for the purpose of in vivo application in humans, clinical applications or therapeutic use.

NOTE International, national or regional regulations or requirements or multiple of them can also apply to specific topics covered in this document.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 8601-1, *Date and time — Representations for information interchange — Part 1: Basic rules*

ISO 20387:2018, *Biotechnology — Biobanking — General requirements for biobanking*

ISO 21709:2020, *Biotechnology — Biobanking — Process and quality requirements for establishment, maintenance and characterization of mammalian cell lines*

ISO 24603:2022, *Biotechnology — Biobanking — Requirements for human and mouse pluripotent stem cells*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 20387, ISO 21709 and the following apply.

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1
authenticity
quality of being genuine or true

[SOURCE: ISO/TS 22859:2022, 3.1]

3.2
biobank
legal entity or part of a legal entity that performs *biobanking* (3.3)

[SOURCE: ISO 20387:2018, 3.5]

3.3
biobanking
process of acquisitioning and storing, together with some or all of the activities related to collection, preparation, preservation, testing, analyzing and distributing defined biological material as well as related information and data

[SOURCE: ISO 20387:2018, 3.6]

3.4
biorisk
effect of uncertainty expressed by the combination of the consequences of an event (including changes in circumstances) and the associated "likelihood" (as defined in ISO Guide 73) of occurrence, where biological material is the source of harm

Note 1 to entry: The harm can be the consequence of an unintentional exposure, accidental release or loss, theft, misuse, diversion, unauthorized access or intentional unauthorized release.

[SOURCE: ISO 35001:2019, 3.17]

3.5
cell culture
growth of cells dissociated from the parent tissue by spontaneous migration, mechanical or enzymatic dispersal for propagation under in vitro conditions

[SOURCE: ISO/TS 22859:2022, 3.5]

3.6
cell master file
complete dossier of all procedures and records used to generate cells

[SOURCE: ISO/TS 22859:2022, 3.6]

3.7
cell morphology
form and structure of the cell

Note 1 to entry: Morphology can be represented by a single parameter or a combination of two or more parameters.

[SOURCE: ISO 21709:2020, 3.3]

3.8
cell population purity
percentage of a particular cell type in a population, of which has the same specific biological characteristics, such as cell specific markers, genetic polymorphisms and biological activities

[SOURCE: ISO/TS 22859:2022, 3.8]

3.9
cryopreservation
process by which cells are maintained frozen at an ultra-low temperature in an inactive state so that they can be revived at a later time

[SOURCE: ISO 21709:2020/Amd.1, 3.6]

3.10
differentiation
process to bring the stem cells into a defined cell state/fate

[SOURCE: ISO/TS 22859:2022, 3.11]

3.11
differentiation potential
ability that refers to the concept that stem and progenitor cells can produce daughter cells which are able to further differentiate into other cell types

[SOURCE: ISO/TS 22859:2022, 3.12]

3.12
flow cytometry
methodologically oriented subdiscipline of analytical cytology that measures cells in suspension in a liquid vehicle as they pass, typically one cell at a time, by a measurement station

Note 1 to entry: The measurement represents transformations of changes in the output of a detector (or detectors) due to changes in scattered light, absorbed light, light emitted (fluorescence) by the cell, or changes in electrical impedance, as the cell passes through the measuring station.

Note 2 to entry: Flow cytometry allows simultaneous evaluation of morphological characteristics of cells (size and internal complexity) with membrane or intracellular antigens.

[SOURCE: ISO/TS 22859:2022, 3.13]

3.13
human neural stem cells derived from pluripotent stem cells
hPSC-NSCs
immature cellular population differentiated from pluripotent stem cells, which has the ability for self-renewal and differentiation to neurons and glia cells (astrocytes or oligodendrocyte) in vitro and in vivo.

Note 1 to entry: Without any manipulation, culture-adapted hNSCs (human neural stem cells) is an alternate term used to denote cells that are different from cells that are found in vivo. It is increasingly clear that these cell types have different properties in terms of gene expression, functionality and phenotype.

3.14
identity verification
part of the process of verifying authenticity of a cell line in which cell origin is genetically confirmed

[SOURCE: ISO 21709:2020, 3.10]

3.15
multipotent cells
cells that have the ability to differentiate into more than one, but a limited number of related cell types

3.16
passage
subculture
process of further culturing of cells in a new culture vessel to provide higher surface area/volume for the cells to grow

[SOURCE: ISO/TS 22859:2022, 3.18]

3.17
passage number
number of subculturings that occurred

Note 1 to entry: For this document P_0 is understood as the starting population of the cells.

[SOURCE: ISO 21709:2020, 3.13, modified — Note 1 to entry has been added.]

3.18
doubling time
PDT
population doubling time
time taken for cultured cell count to double

Note 1 to entry: The time is measured in hours.

[SOURCE: ISO 21709:2020, 3.8, modified — “population doubling time” and “PDT” have been added as the preferred term and Note 1 to entry has been added.]

3.19
primary cells
cells isolated directly from body fluid, tissue or organs taken directly from an organism, using enzymatic or mechanical methods

[SOURCE: ISO 21709:2020, 3.15, modified — "body fluid" added to definition.]

3.20
primary culture
initial in vitro cultivation of *primary cells* (3.19)

3.21
primary human neural stem cells derived from pluripotent stem cells
primary hPSC-NSCs
initial neural stem cells (NSCs) derived from in vitro human pluripotent stem cell (hPSC) differentiation

3.22
proliferation
cell number expansion by cell division

[SOURCE: ISO/TS 22859:2022, 3.22]

3.23
self-renewal
ability of *stem cells* (3.24) to divide symmetrically, forming two identical daughter stem cells

Note 1 to entry: Adult stem cells like neural stem cell, bone marrow stem cell etc. can also divide asymmetrically to form one daughter cell which can proceed irreversibly to a differentiated cell lineage and ultimately lead to focused functional differentiated cells, whilst the other daughter cell still retains the characteristics of the parental stem cell.

[SOURCE: ISO/TS 22859:2022, 3.23]

3.24
stem cell
non-specialized cells with the capacity for *self-renewal* (3.23) and *differentiation potential* (3.11), which can differentiate into one or more different types of specialized cells

Note 1 to entry: Most adult stem cells are multipotent stem cells.

[SOURCE: ISO/TS 22859:2022, 3.24]

3.25
viability
attribute of being alive (e.g., metabolically active, capable of reproducing, have intact cell membrane, or have the capacity to resume these functions) as defined based on the intended use

[SOURCE: ISO 21709:2020, 3.17]

3.26
viable cells
cells within a sample that have an attribute of being alive (e.g. metabolically active, capable of reproduction, possessed of intact cell membrane, or with the capacity to resume these functions) defined based on the intended use

[SOURCE: ISO 20391-1:2018, 3.29]

4 Abbreviations

Abbreviation	Term
AD	Alzheimer's disease
ALS	amyotrophic lateral sclerosis
B27	The most cited neural cell culture supplement, which is an optimized serum-free supplement used to support the neural cell culture
BDNF	brain-derived neurotrophic factor
bFGF	basic fibroblast growth factor
BMP	bone morphogenetic protein
CFSE	carboxyfluorescein succinimidyl ester
CNS	central nervous system
CORIN	atrial natriuretic peptide-converting enzyme
DCX	doublecortin
DG	dentate gyrus
DMEM/F-12	Dulbecco's Modified Eagle Medium/Nutrient Mixture F-12
EB	embryoid body
EDTA	ethylene diamine tetraacetic acid
EGF	epidermal growth factor
ELISA	enzyme-linked immunosorbent assay
FACS	fluorescence-activated cell sorting
FBS	fetal bovine serum
FL	fluorescence spectrophotometer
FOXA2	forkhead box protein A2
GABA	gamma-aminobutyric acid
GPCs	GABA-ergic progenitor cells
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCsAg	hepatitis C surface antigen
HCV	hepatitis C virus
HIV	human immunodeficiency virus
hPSC-NSCs	hPSC derived NSCs
hPSC	pluripotent stem cell
IPC	intermediate progenitor cell
KOSR	KnockOut™ [a] Serum Replacement
Lif	leukemia inhibitor factor
MNs	motor nuerons

[a] KnockOut™ Serum Replacement is a trademark of ThermoFisher Scientific. This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of the product named.

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