International Standard

ISO 20012

Biotechnology — Biobanking — Requirements for human natural killer cells derived from pluripotent stem cells

Biotechnologie — Mise en banque de matériel biologique — Exigences relatives aux cellules tueuses naturelles humaines dérivées de cellules souches pluripotentes

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ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: www.iso.org

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Foreword

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This document was prepared by Technical Committee 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

Natural killer (NK) cells, also known as large granular lymphocytes (LGL), are a type of cytotoxic lymphocytes belonging to the innate immune system. NK cells constitute 5 % to 15 % of the mononuclear cells and up to 20 % of lymphocytic population[1] in the peripheral blood. The expression patterns of activating receptors and inhibitory receptors determine the activating status and functionalities of NK cells. NK cells can eliminate pathogen-infected cells, cancerous cells, and other unhealthy cells by direct cytotoxicity. They express apoptosis-related ligands (TRAIL and FasL) and cytotoxic granules (granzymes and perforin) which can induce cell death in stressed cells. NK cells with the expression of CD16 can also kill antibody-coated target cells by antibody-dependent cell cytotoxicity (ADCC). As innate immune cells, NK cells are also engaged in reciprocal interactions with other immune cells to limit or exacerbate immune responses[2].

In adult, hematopoietic stem cells (HSCs) differentiate into common lymphoid progenitors (CLPs), then, give rise to NK progenitors (NKP). NKPs migrate into all lymphoid tissues or organs, and differentiate into mature NK cells subsequently[3]. However, NK cells can also arise from erythro-myeloid progenitors (EMPs) in the yolk sac. NK cells can be generated by induction from human pluripotent stem cells (hPSCs)[4]. Regarding the various tissue origins of natural NK cells during development, there also has been established various methods for generating induced NK cells from hPSCs. In the NK cell regeneration system, hPSCs are first induced into mesoderm progenitors or lateral plate mesoderm cells via embryo body (EB) formation or monolayer differentiation methods. Then, these cells can be induced into hemogenic endothelial cells (HECs) which further differentiate into hematopoietic progenitor cells (HPCs) via hematopoietic transition (EHT). NK cells can even totally regenerated from these HPCs under specified cytokine combinations[5],[6].

NK cells are fragile and sensitive to cryopreservation and thawing. Standardized approaches to maintain the functionality of banked NK cells is needed. hPSC-dervied NK cell are primary cells, not immortalized, and therefore have a finite life span.

This document is applicable for academic centers, public and private institutions performing NK cell generation from hPSCs (Research and Development) and preclinical studies, not for clinical use.

Importantly, this document is focused on NK cell regeneration that have been reported from hPSCs in culture for research purposes.

EXAMPLE Applications of NK cells (e.g. immunoresponse regulation, anti-tumor or anti-viral)

Biotechnology — Biobanking — Requirements for human natural killer cells derived from pluripotent stem cells

1 Scope

This document specifies requirements for the biobanking of human natural killer (NK) cells derived from human pluripotent stem cells (hPSCs), including the requirements for the differentiaton, culture, characterization, quality control, storage, thawing and transport of NK cells.

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 human NK cells used for research and development in the life sciences.

This document does not apply to human NK cells 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, *Biotechnology — Biobanking — General requirements for biobanks*

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

ISO/TS 23511, *Biotechnology — General requirements and considerations for cell line authentication*

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

ISO 24190, *Biotechnology — Analytical methods — Risk-based approach for method selection and validation for rapid microbial detection in bioprocesses*

ISO 35001, *Biorisk management for laboratories and other related organisations*

ISO 35001:2019/Amd 1:2024, *Biorisk management for laboratories and other related organisations — Amendment 1: Climate action changes*

ISO 8934-1, *Cell viability analytical methods — Part 1: General requirements and considerations*

3 Terms and definitions

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