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Company Name: HEALIOS K.K.
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(TSE Growth Code: 4593)

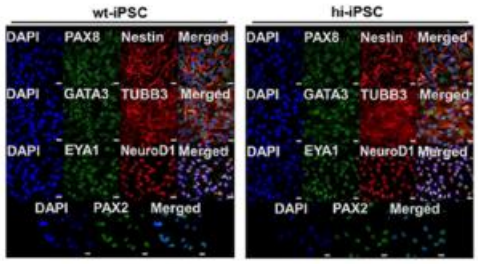
Healios UDC-derived otic neural progenitor cells demonstrate enhanced survival after transplantation into the cochlea: Northwestern University publication

HEALIOS K.K. ("Healios") is involved in the research of new therapeutic products using Universal Donor Cells ("UDCs")*, which are next-generation iPS cells created with gene-editing technology that have a reduced risk of immune rejection regardless of a patient's HLA type. A research team led by Dr. A. J. Matsuoka of Northwestern University (Chicago, IL, USA) has confirmed that otic neural progenitor cells differentiated from UDCs produced by Healios showed enhanced survival after transplantation into the cochlea compared to otic neural progenitor cells differentiated from an unmodified parental cell line. Healios is pleased to announce that a paper on this research has been published in Stem Cell Research & Therapy, a scientific and academic research journal.

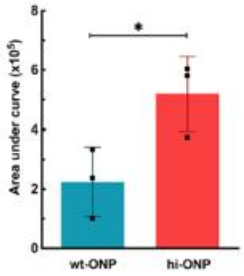
Title:
Enhanced survival of hypoimmunogenic otic progenitors following intracochlear xenotransplantation: repercussions for stem cell therapy in hearing loss models

Abstract:
Stem cell replacement holds the potential for sensorineural hearing loss (SNHL) treatment. However, its translation into clinical practice requires strategies for improving stem cell survival following intracochlear transplantation. Considering recent findings showing that the inner ear contains a resident population of immune cells, we hypothesized that immune evasion would improve the survival and residence time of transplanted stem cells in the cochlea, potentially leading to better outcomes. To test this, we leveraged genetic engineering techniques to develop hypoimmunogenic human-induced pluripotent stem cells (hi-iPSCs), which lack human leukocyte antigen expression. We found that gene editing does not affect the biological properties of hi-iPSCs, including their capacity to differentiate into otic neural progenitors (ONPs). Compared to wild-type ONPs, more hypoimmunogenic ONPs (derived from hi-iPSCs) were found in the inner ear of immunocompetent mice ten days following cochlear xenotransplantation. This approach may open a new avenue for experimental and clinical SNHL treatments.

In this paper Healios UDCs (hi-iPSCs) differentiated into late-stage ONPs as well as unedited cells (wt-iPSC) using multiple differentiation markers. More UDC-derived ONPs (hi-ONPs) than unedited parental cell-derived ONPs (wt-ONPs) were viable after transplantation. In other words, immune rejection was reduced as expected.



Representative immunocytochemistry photomicrographs of iPSC-derived ONPs



Quantification of iPSC-derived ONPs 10 days following intracochlear transplantation

(Source: Northwestern University)

Healios has confirmed that UDCs are capable of differentiation into various cells, such as photoreceptor cells and pancreatic beta cells. The induction of differentiation into otic neural progenitor cells and the hypo-immune benefit upon transplantation into mice were confirmed, further advancing the potential of UDCs as a next-generation technology platform for the creation of regenerative medicine products.

* UDCs
UDCs are iPS cells created using gene-editing technology that allows them to avoid and / or reduce the body's immune rejection response. The production of Healios' UDCs involve the removal of certain HLA genes that elicit a rejection response and the introduction of certain genes to improve immune evasion and safety in an allogeneic iPS cell. This next-generation technology platform allows for the creation of regenerative medicine products with enhanced safety and a lower risk of immune rejection, while preserving the inherent ability of iPS cells to replicate themselves continuously and their pluripotency in differentiating into various other kinds of cells.

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