Docket #: S22-419

Method for generating human spiral ganglion neurons

Spiral ganglion neurons (SGNs) are essential for hearing as they transmit electrical signals from the cochlea to the brain. Loss of SGNs causes permanent hearing loss because SGNs do not spontaneously regenerate in humans. Despite their scientific and clinical importance, the developmental, cellular, and molecular features of human SGNs remain poorly characterized due to the limited accessibility to the human inner ear and incomplete phenotypic conversion of stem cells into SGN-like cells in vitro. Unfortunately, a fundamental obstacle in the study of human SGNs is the inability to obtain routine tissue biopsies due to the small size of the cochlea, its complex three-dimensional anatomy, and encasement in dense bone.

To overcome this challenge, inventors at Stanford have developed a novel method for generating human spiral ganglion neurons using human-induced pluripotent stem cells (hiPSCs) to generate functional SGNs via otic neurosensory progenitor cells (ONPs) in vitro. Utilizing the method enables the mimicking of in vivo cell-to-cell signaling occurring during human inner ear development. This is the first comprehensive description of the heterogeneity of human auditory neuronal populations using high-resolution transcriptomic profiling of individual cells, coupled with electrophysiological characterization of the cells' functional diversification. These human neurons offer powerful cellular models to decipher the precise mechanisms underlying hearing disorders and to enable future targeted therapies.

The invention offers a novel platform to answer fundamental questions in auditory research and facilitate therapeutic innovation for sensorineural hearing loss. The high-efficiency, monolayer SGN culture protocol could be a reliable source of cells for drug screening. Unlike 3D organoids, the invented method results in 2D cultures that are representative of their in vivo counterparts and provide benefits for easier scale-up, monitoring, functional tests, and quality control in a realistic way, as has already been demonstrated using dissociated mouse SGNs. Finally, this protocol could be used to test potentially regenerative, patient-specific therapies aimed at replacing or

repairing human SGNs.

Applications

- Therapeutic innovation for sensorineural hearing loss
- Understanding of the normal, as well as abnormal, development of the human auditory system
- Understanding inherited disorders leading to hearing loss.
- Drug screening
- 2D in vivo cultures for easier scale-up, monitoring, functional tests, and quality control
- Regenerative, patient-specific therapies aimed at replacing or repairing human SGNs

Advantages

- Novel platform to answer fundamental questions in auditory research and facilitate therapeutic innovation for sensorineural hearing loss
- 2D cultures for easier scale-up, monitoring, functional tests, and quality control of high-throughput drug screening
- First comprehensive description of the heterogeneity of human auditory neuronal populations using high-resolution transcriptomic profiling of individual cells, coupled with electrophysiological characterization of the cells' functional diversification.

Patents

- Published Application: WO2026193435

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