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Azel Zine et al, J Stem Cell Res Ther 2018, Volume 8
DOI: 10.4172/2157-7633-C5-044

Migration, integration and differentiation of human induced pluripotent stem cell-derived otic progenitors following transplantation in animal model of sensorineural hearing loss

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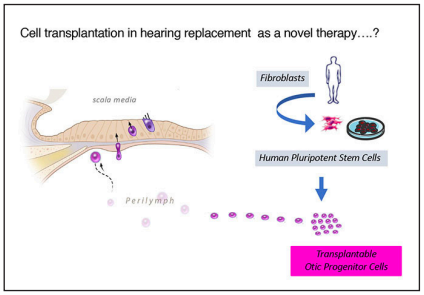

Deafness is a major public health issue and the most common sensory deficit in humans. Approximately 360 million people have disabling hearing losses, a number likely to grow due to increasing noise pollution, ototoxic drugs and aging. Most forms of deafness are progressive and neurodegenerative disorders involving the loss of sensory hair cells and their associated primary auditory neurons. These sensory cells are not replaced and hearing loss is permanent. A stem cell-based therapy could in principle offers reasonable expectations for the potential treatment of inner ear disorders through the replacement of lost or damaged sensory cells. Initial advances in the differentiation of murine ESCs/iPSCs into hair cell and neuron-like cells have paved the way for similar progresses with human pluripotent stem cells. In this study, we used monolayer cultures, exposure to otic-inducing agents, Notch signaling modulation, and cell type marker expression to obtain characterized human otic/placodal progenitors from human induced Pluripotent Stem Cells (hiPSCs). Then, we explored the engraftment ability of in vitro generated human otic progenitor cells in experimental model of sensorineural hearing loss. The results from our study indicate that hiPSC-derived otic/placodal progenitor cells survived up to one month after transplantation, migrated and integrated into the endogenous cochlear epithelium of in vivo ototoxic model of hearing loss. Once within the microenvironment of the ototoxic damaged cochlea, some of the injected human otic progenitor's up regulate a subset of initial inner ear sensory cell type markers. Information's provided by the experiments of this study would bring the possibility of using a stem cell-based cell therapy as a potential option for deafness closer to becoming reality and pave the way for clinical trials in human.

Biography

Azel Zine has his expertise in the study of development and regeneration of the peripheral auditory system. He has made seminal contributions to our understanding of the Notch signaling and *HES* gene roles in the development of auditory hair cells in mammals. His scientific contributions have all been well thought out and comprehensive, published in some of highly peer reviewed journals. His work with applying the degradation resistant JNK inhibitor (D-JNK-1) to the inner ear as an otoprotective drug has also been notable and the results reported in that initial work has led to clinical trials in Europe that are in progress under the direction of Auris Medical-Biotechnology Company. His current research is in the field of stem cells biology.

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