Stem cell transplantation into mouse cochlea may impact future hearing loss therapies

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Researchers in Japan who evaluated the risks and efficacy of transplanting two varieties of stem cells into mouse cochlea have concluded that both adult-derived induced pluripotent stem (iPS) cells and mouse embryonic stem (ES) cells demonstrate similar survival and neural differentiation capabilities. However, there is a risk of tumor growth associated with transplanting iPS cells into mouse cochleae. Given the potential for tumorigenesis, they concluded that the source of iPS cells is a critical issue for iPS cell-based therapy.

Their study is published in a recent issue of *Cell Transplantation* (21:4), now freely available online.

"Hearing loss affects millions of people worldwide," said Dr. Takayuki Nakagawa of the Department of Otolaryngology, Graduate School of Medicine, Kyoto University, Japan. "Recent studies have indicated the potential of stem-cell based approaches for the regeneration of hair cells and associated auditory primary neurons. These structures are essential for hearing and defects result in profound hearing loss and deafness."

The authors noted that embryonic stem cells have previously been identified as promising candidates for transplantation, however they have also been associated with immune rejection and ethics issues. Consequently, this study compared the survival and neural differentiation capabilities of ES and three clones of mouse iPS cells.

"Our study examined using induced pluripotent stem cells generated

from the patient source to determine if they offer a promising alternative to ES cells," explained Dr. Nakagawa. "In addition, the potential for tumor risk from iPS cells needed clarification."

Four weeks after transplantation, the researchers found that the majority of cochleae that had been transplanted exhibited the settlement of iPS or ES-derived neurons. However, there was a difference in the number of cells present based on cell lines. They noted that the number of cells able to be transplanted into cochleae is limited because of the cochleae's tiny size. Thus, the number of settled cells is low.

They also noted the formation of a teratoma (encapsulated tumor) in some cochlea after transplantation with one group of iPS cells.

"To our knowledge, this is the first documentation of teratoma formation in cochleae after cell transplantation," said Dr. Nakagawa.

The researchers concluded that the teratoma formation in one iPS cell line indicated the necessity for selecting appropriate iPS cell lines for avoiding tumorigenesis. They also noted the need for developing methods to eliminate undifferentiated cells after neural induction in order to establish safe iPS-based therapy for the inner ear.

"While this study did not look at the ability of the transplanted cells to repair hearing loss, it does provide insight into the survival and fate of transplanted cells. It highlights the importance of factors such as knowing the original source of the cells and their degree of undifferentiation to enable the cells to be ranked in order of their likelihood of forming tumors" said Dr. John Sladek, professor of neurology and pediatrics at the University of Colorado School of Medicine.

More information: Nishimura, K.; Nakagawa, T.; Sakamoto, T.; Ito, J.

Fates of murine pluripotent stem cell-derived neural progenitors following transplantation into mouse cochleae. *Cell Transplant.* 21(4):763-771; 2012.

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