

## Prospects of Regenerative Medicine with Human Allogeneic Adipose Tissue-Derived Mesenchymal Stem Cell Sheets: Achievements and Future Outlook in Clinical Trials for Myopic Chorioretinal Atrophy

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**Abstract :** Mesenchymal stem cells are thought to confer neuroprotection, facilitate tissue regeneration and exert their effects on retinal degenerative diseases, however, adverse events such as proliferative vitreoretinopathy and preretinal membrane disease associated with cell suspension transplantation have also been reported. We have recently developed human (allogeneic) adipose tissue-derived mesenchymal stem cell (adMSC) sheets through our proprietary sheet transformation technique, which could potentially mitigate these adverse events. To clarify the properties of our adMSC sheets named PAL-222, we performed in vitro studies such as viability testing, cytokine secretions by ELISA, immunohistochemical study, and migration assay. The viability of the cells exceeded 70%. Vascular Endothelial Growth Factor (VEGF) and Pigment Epithelium-Derived Factor (PEDF), which are quite important cytokines for the retinal area, were observed. PAL-222 expressed type I collagen, a strength marker, type IV collagen, a marker of the basement membrane, and elastin, an elasticity marker. Finally, the migration assay was performed and showed negative, which means that PAL-222 is stably kept in the topical area and does not come to pieces. Next, to evaluate the efficacy in vivo, we transplanted PAL-222 into the subretinal space of the eye of Royal College of Surgeons rats with congenital retinal degeneration and assessed it for three weeks after transplantation. We confirmed that PAL-222 suppressed the decrease in the thickness of the outer nuclear layer, which means that the photoreceptor protective effect treated with PAL-222 was significantly higher than that in the sham group. ( $p < 0.01$ ). This finding demonstrates that PAL-222 showed their retinoprotective effect in a model of congenital retinal degeneration. As the study suggested the efficacy of PAL-222 in both in vitro and in vivo studies, we are presently engaged in clinical trials of PAL-222 for myopic chorioretinal atrophy, which is one of the retinal degenerative diseases, for the purpose of regenerative medicine.

**Keywords :** cell sheet, clinical trial, mesenchymal stem cell, myopic chorioretinal atrophy

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