AGE-RELATED MACULAR DEGENERATION (WET TYPE)

INTRODUCTION

Wet age-related macular degeneration (AMD) is characterized by the ectopic growth of new immature blood vessels into the subretinal space (choroidal neovascularization: CNV), which causes haemorrhage and exudative changes and irreversibly damages retinal neurons. The current first-line therapy is the repeated injection of anti-vascular endothelial growth factor (anti-VEGF) drugs into the eye, but about half the patients require continual injections to prevent the disease from coming back. One primary therapy would be the removal of CNV but it often leads to the loss of retinal pigment epithelial cells (RPEs) that were attached to it. RPEs are essential for the maintenance of a healthy neural retina. Therefore, together with inhibition or removal of CNV, replacement of healthy RPE cells is a rational approach to maintain vision in this condition.

RATIONALE FOR USING CELL BASED THERAPIES FOR AMD

Initially, the transplantation of the patients' own RPE, harvested in sheets from the peripheral part of the eye and placed sub-retinally after removal of CNV, was shown to be effective in some patients. However, overall, the surgical procedure of harvesting an RPE sheet and placing it in the macular area is quite invasive and it would be better if the transplant came from another source. This provides the rationale for transplanting pluripotent stem cell-derived RPE sheets prepared ex vivo after removal of CNV.

WHERE ARE WE WITH CELL BASED THERAPIES FOR WET AMD?

Cell based therapy using embryonic stem (ES) cell-derived RPE transplantation was first tested in dry AMD[1,] followed by two clinical investigations of ES- and induced pluripotent stem (iPS) cell derived-RPE sheet transplantation for wet AMD [2,3]. These studies have shown that pluripotent stem cell derived-RPE transplantation can be done safely and is feasible. The efficacy of this approach is still being investigated and will determine whether this therapy becomes a standard of care for this condition.

WHERE DO TRIALS STAND?

Another clinical trial using HLA-matched iPS-derived RPE transplants for wet AMD is currently under way. Other clinical trials are expected to start in near future to assess the efficacy of this approach in other diseases involving RPE atrophy.

REFERENCES

1. Schwartz SD, Regillo CD, Lam BL, et al. Human embryonic stem cell-derived retinal pigment epithelium in patients with age-related macular degeneration and Stargardt's macular dystrophy: follow-up of two open-label phase 1/2 studies. The Lancet 2015;385:509-516.
2. Kashani AH, Lebkowski JS, Rahhal FM, et al. A bioengineered retinal pigment epithelial monolayer for advanced, dry age-related macular degeneration. Sci Transl Med 2018;10(435).
3. Mandai M, Watanabe A, Kurimoto Y, et al. Autologous Induced Stem-Cell-Derived Retinal Cells for Macular Degeneration. N Engl J Med 2017;376:1038-1046.

Masayo Takahashi, MD, PhD, Riken Center for Developmental Biology and the ISSCR Clinical Translation Committee

March 2019