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Improved transduction efficiencies of modified *Volvox*-derived channelrhodopsin-1 gene by synthetic cell-permeable peptides

Hiroshi Tomita
Iwate University, Japan

We have been researching gene therapy using AAV for blind patients with Retinitis Pigmentosa (RP) using optogenetic technology. Recently, we succeeded in developing a new type of optogenetic gene, mVChR1, which has different wavelength sensitivity from that of other channelrhodopsins, and safety studies have also been performed for this gene. On the other hands, visual function restored by gene therapy depends on transduction efficiency. Therefore, it is important to improve the transduction efficiency of AAV-mediated gene therapy. The AAV type-2 vector has been used successfully in human gene therapies. However, the transduction efficiency of AAV2 depends on the cell type, and this poses a problem in the efficacy of gene therapy. To improve the transduction efficiency of AAV2, we designed a small peptide consisting of epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor peptide and the HIV-Tat sequence Tat-Y1068. Pre- or co-treatment of CYNOM-K1 cells from cynomolgus monkey embryo skin with Tat-Y1068 increased the transduction efficiencies in a dose-dependent manner and caused p38 phosphorylation. The transduction efficiency of AAV2 into the rat fibroblast cell line RAT-1 highly expressing EGFR was less than the transduction efficiency of AAV2 into CYNOM-K1 cells. Tat-Y1068 increased the transduction efficiency in RAT-1 cells in the same manner as in CYNOM-K1 cells. In conclusion, cell-permeable peptides possessing the EGFR tyrosine kinase inhibitor function might serve as a useful ingredient of AAV2 vector solution for increasing the transduction efficiency of gene therapies.

Biography

Hiroshi Tomita has completed his PhD from Tohoku University and Post-doctoral studies from Oklahoma University School of Medicine. He is the Professor of Iwate University. He has published more than 60 papers in reputed journals and has been serving as an Editorial Board Member of repute.

htomita@iwate-u.ac.jp

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