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Analysis of adverse effect caused by AAV-2 encoded modified Volvox channelrhdopsin-1 gene therapy

Eriko Sugano Iwate University, Japan

We designed a modified channelrhodopsin-1 (mVChR1) protein chimera, which has a broader, red-shifted action spectrum than that of *Chlamydomonas* channelrhodopsin-2. We previously reported that its transduction into retinal ganglion cells could restore visual function in genetically blind rats with photostimuli ranging from 486 to 640 nm. However, it has the possibility that mVChR1-mediated gene therapy causes some adverse effects such as immune response because of the use of the non-human gene. To investigate the safety and influence of mVChR1 transgene expression, adeno-associated virus type-2 encoding mVChR1 was administered by intra-vitreous injection into genetically blind rats. Reverse-transcription PCR was used to monitor transgene dissemination to non-targeted organs and the results demonstrated that their expression was restricted specifically within the eye tissues. Moreover, no excess immunoreactivity was present in standard clinical hematological parameters of plasma and serum. Serum antibodies targeting the recombinant adeno associated virus (rAAV) capsid increased after the injection; however, no increase in mVChR1 antibody was detected during for 10 months after the injection. In addition, retinal histological examination showed no signs of inflammation in rAAV-injected rats. In conclusion, our results demonstrate that mVChR1 can be exogenously expressed without harmful immunological reactions *in vivo*. These findings will help the optogenetic approach for restoration of vision in late-stage retinitis pigmentosa.

Biography

Eriko Sugano has worked as a Researcher in Tohoku University School of Medicine in Japan and received PhD from Tohoku University in Life science. She has worked as an Instructor in Biomedical Engineering Research Organization and International Advanced Interdisciplinary Research, Tohoku University. She is the Associate Professor of Chemistry and Biological Sciences, Iwate University. She has published more than 30 papers in reputed journals.

sseriko@iwate-u.ac.jp

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