

Stem cell therapy for glaucoma—there is still a long way to go

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Provenance: This is a Guest Perspective commissioned by Section Editor Kangjun Li, PhD student (State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China).

Comment on: Sluch VM, Davis CH, Ranganathan V, *et al.* Differentiation of human ESCs to retinal ganglion cells using a CRISPR engineered reporter cell line. *Sci Rep* 2015;5:16595.

Abstract: Glaucoma is now the second leading reason of blindness in the world and is characterized by gradual loss of retinal ganglion cells. Stem cells have the ability to regenerate human structures. Although there are still problems unsolved, stem cell therapy might provide brighter future for treatment of glaucoma.

Keywords: Stem cell therapy; glaucoma

Received: 22 December 2016; Accepted: 23 December 2016; Published: 16 February 2017.

doi: 10.21037/aes.2017.01.07

View this article at: <http://dx.doi.org/10.21037/aes.2017.01.07>

Glaucoma is now the second leading reason of blindness in the world and is characterized by elevated intraocular pressure and gradual loss of vision (1).

A recently published article by Zack *et al.* showed us a novel way of harvesting RGC cells from embryonic stem cells. Utilization of CRISPR-Cas9 in the experiment granted a simple, adherent cell culture protocol for differentiation of hPSCs to RGCs *in vitro*. CRISPR engineered ESCs showed high success rate of developing into RGCs and specific markers as well as characters of RGCs.

It seemed this novel method has provided us with a brighter beginning on the way of RGC regenerating with CRISPR technique, however, there is still a long way to go.

Firstly, CRISPR-Cas9 is still not widely used worldwide and has a lot of limitations. CRISPR is only to be used in embryos, which brings ethical issues. Besides, success rate of inserting new gene segments into specific location in human genome by CRISPR technique is low and unstable. Thus it won't be easy for everyone to repeat the result in the study mentioned above.

Secondly, impairment of RGCs in patients with glaucoma is different from that in patients with ocular trauma. The latter causes direct damage to optic nerve,

leading to vision loss. However, glaucomatous damage of optic nerve is gradual and silent. And it's hard to detect a clear anatomical abnormality of optic nerve in glaucoma. So re-growth of axon and redirection of axon to its original spatial position is quite hard. Without accurate localization of axon back to the central nervous system (CNS), it's impossible for patients to regain their lost vision.

Thirdly, previous studies showed sometimes although axons grew back to their original place, they were not functional (2). No improvement in vision was observed, which means the communication between regrown axon and CNS was not successfully built. And this is the biggest obstruction we are faced with.

In a word, it's meaningful to discover new and easier way to regenerating RGCs. But more importantly, the immortal theme about RGC regeneration is regaining function. Building up a correct anatomical structure is just the first step, and the second step needs further investigation.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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doi: 10.21037/aes.2017.01.07

Cite this article as: Li F, Zhang X. Stem cell therapy for glaucoma—there is still a long way to go. *Ann Eye Sci* 2017;2:13.