OMICS Group Conferences
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International Conference on
Emerging Cell Therapies

October 1-3, 2012 DoubleTree by Hilton Chicago-North Shore, USA

Towards in situ photoreceptor replacement in the mammalian eye

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Recently success of rescuing vision by photoreceptor replacement in mouse models of photoreceptor degeneration intensifies the need to generate/regenerate photoreceptor neurons for cell replacement therapies. Current research on producing mammalian photoreceptor neurons, as regenerative medicine in general, focuses on the use of ES cells and iPS cells. Nonetheless, a naturally occurring way of regeneration, such as wound healing, involves awakening cells at the site of a wound to produce new cells needed to heal the wound. We are exploring this natural way in our quest of inducing photoreceptor regeneration in the mammalian eye. Our study takes advantage of the wound healing ability of the retinal pigment epithelium (RPE), a non-neural epithelium adjacent to the retinal photoreceptor neurons, and uses a pro-photoreceptor gene (ngn1 or ngn3) to reprogram the RPE to produce new photoreceptor cells. Transgenic (Tg) mice were generated with a DNA construct, in which RPE bestrophin-1 promoter would drive the expression of ngn1 or ngn3. BrdU incorporation, coupled with double-labeling for a photoreceptor protein and morphological and histological criteria, was used to identify new-born photoreceptor cells and as an indicator of photoreceptor regeneration. Double-labeled cells were found in adult Tg mice. Double-labeled cells were also found in animals from crossing Tg with rd1 mice, whose photoreceptors undergo rapid degeneration soon after maturation. Our results suggest photoreceptor regeneration taking place in adult Tg mice and point to a way to regenerate photoreceptor cells in the mammalian eye for cell replacement without the involvement of cell transplantation.

Biography

Shu-Zhen Wang, PhD, began her study of retinal genesis at Wilmer Eye Institute of the Johns Hopkins School of Medline. Dr. Wang is currently on faculty of the University of Alabama at Birmingham School of Medicine. Her research is/was supported by the National Eye Institute of the National Institutes of Health, the EyeSight Foundation of Alabama, the International Retinal Research Foundation, and the Research to Prevent Blindness. Dr. Wang has served on various national and international review panels of research grants. She has reviewed manuscripts for a number of scientific journals and recently served as Editor of Retinal Development: Methods and Protocols, Methods in Molecular Biology, Springer Protocols (Humana Press).

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