

Generating photoreceptors from stem cells

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Purpose: Our published results have shown that retinal stem cells (RSCs) can be isolated from radial glia-like cells of the newborn mouse retina (Angénioux et al., 2006). These RSCs have great capacity to renew and generate neurons including cells differentiated towards the photoreceptor lineage (Mehri-Soussi et al., 2006). However, the lineage relationship between radial glia and photoreceptors remains unclear.

Setting/Venue: Determine whether the generation of photoreceptor cells by radial glia-like cells or glial cells occurs during neurogenesis or whether a transdifferentiation/stochastic phenomenon takes place.

Methods: Different models are proposed to identify the relationship between radial glia and photoreceptor cells. 3D culture system is used to determine whether radial glia in vitro have characteristics of retinal stem cells in vivo. GLAST-desRed::Crx-GFP mouse retina and retinal cells serve to follow simultaneously the fate of radial glia and photoreceptors. Embryonic Stem (ES) cell-derived Radial glia cells were also challenged for their capacity to generate photoreceptor cells.

Results: The dependence of integrin for retinal progenitor stimulation was previously described in vivo. Using self-assembling polymers cross-linked with RGDSP peptides to stimulate integrin receptors, we observed that radial glia positive cells increase their proliferation and migration potentials. The differentiation induces rhodopsin gene expression. Manipulation of ES cells allows the generation of radial glia expressing early retinal markers. Finally, the in vivo analysis of radial glia during early stage of photoreceptor generation reveals a tight interaction between these two cell populations, but no generation of photoreceptor cells derived from radial glia during retinogenesis was observed.

Conclusions: Radial glia show in vitro capability to generate cells expressing photoreceptor genes, but do not seem to participate to neuron formation in the retina during development as they did for certain regions of the brain.

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