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Rhodopsin promoter-EGFP fusion transgene expression in photoreceptor neurons of retina and pineal complex in mice

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Abstract

Light detection in vertebrate eyes is mediated through retinal photoreceptor rod and cone cells that transduce light signals into electrical responses. The differentiation and synaptogenesis of photoreceptor cells are especially important since these cells are the main targets of degeneration in retinitis pigmentosa. We produced transgenic mice that express enhanced green fluorescent protein (EGFP) under the control of the mouse rhodopsin gene promoter. In Western blot analyses of transgenic retinal homogenates, expression of the endogenous rhodopsin gene was detected from post-natal day (P)8; however, EGFP expression in transgenic retinas was initially detected at P12, indicating delayed expression of the transgene. At P14, fluorescence microscopy showed a weak expression of EGFP in the transgenic retina. In the adult transgenic mice, the strongest EGFP expression was observed in the outer nuclear layer, and to a lesser extent in the outer plexiform layer as well as in the inner and outer segments. EGFP expression was also observed in the pineal stalk. The rhodopsin promoter-EGFP transgenic mice will be not only useful to assess rhodopsin gene promoter activity in vivo, but also for retinal transplant studies as a source of functional photoreceptor cells that are fluorescent green.

Keywords: Transgenic mice; EGFP; Photoreceptor; Rhodopsin; Promoter; Retina

The retina has been the target of many developmental studies, because of interest in using the retina as a model for the central nervous system development. Histological studies of mammalian retinal neurogenesis have revealed the processes of neuroepithelial cell development into the highly-organized, multilayered retina [24]. Cell lineage tracing in mammals revealed that retinal progenitor cells are multipotent and retain their ability to generate various cell types such as ganglion cells, horizontal cells, cone-photoreceptors, amacrine cells, rod-photoreceptors, bipolar cells and Müller glia cells [17,28]. Many recent studies are focusing on the transcription factors required for retinal cell diversification [1,3,7,10,18,19,23,25,26]. In many cases of human retinal degenerative disease, photoreceptor cells are the targets of neurodegeneration, while the neurons of the inner retina are well preserved [24].

Rhodopsin, which is present in mature rod-photoreceptor cells, is a 40-kDa transmembrane apoprotein that transduces light signals into a G-protein mediated signal cascade [16]. A point mutation in exon 1 of the human opsin gene has been shown to cause one form of autosomal dominant retinitis pigmentosa [8]. To date, more than 100 mutations in opsin gene which can lead to retinitis pigmentosa are reported (see for example tables in RetNet: http://www.sph.uth.tmc.edu/Retnet/home.htm). Interestingly, rhodopsin-null mice almost completely lose their photoreceptor cells within 3 months after birth [11]. These

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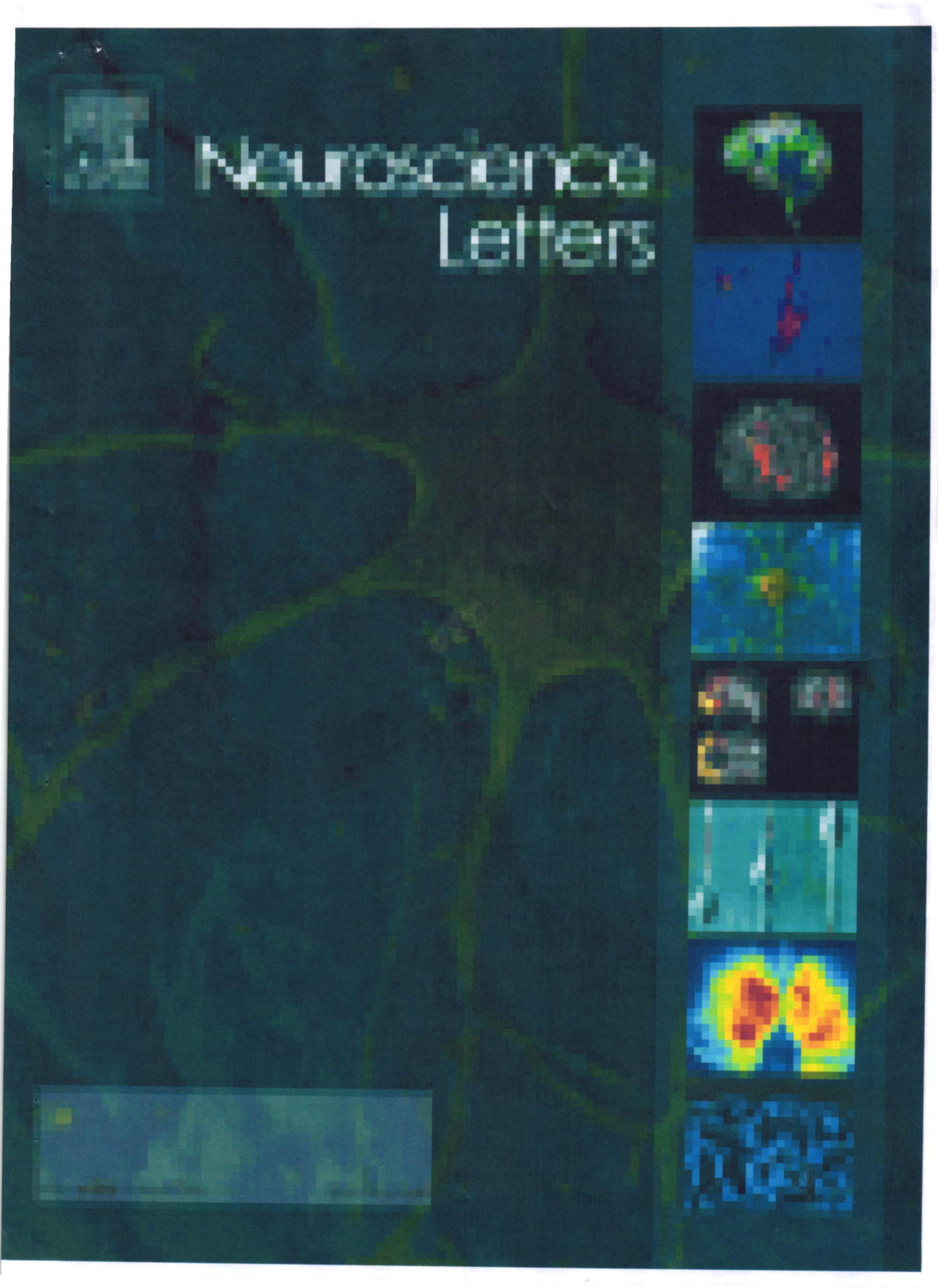
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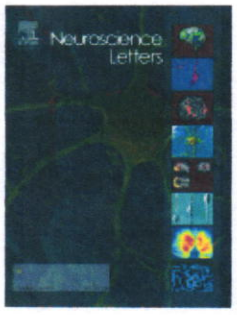

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