Implantation of Mouse Eyes with a Subretinal Microphotodiode Array

Machelle T. Pardue, Tiffany A. Walker, Amanda E. Faulkner, Moon K. Kim, Christopher M. Bonner, and George Y. McLean

1 Introduction

Retinal prosthetics are designed to restore vision in patients with photoreceptor degenerative diseases, such as retinitis pigmentosa (RP) and macular degeneration. Subretinal microphotodiode arrays (MPAs), which response to incident light in a gradient fashion, have been designed to replace degenerating photoreceptors. Such devices have been implanted into rats (Ball et al., 2001), cats (Chow et al., 2001) and humans (Chow et al., 2004). These studies have revealed that implantation of a MPA device is capable of restoring some visual function in patients (Chow et al., 2004) and eliciting a superior colliculus response in normal and degenerating rats (DeMarco et al., 2007). Furthermore, the low level electrical stimulation produced by the MPA device has been shown to have neuroprotective properties (Pardue et al., 2005).

When RCS rats are implanted with an MPA device at the beginning of the degenerative process, photoreceptor function and morphology are preserved (Pardue et al., 2005). Subretinal electrical stimulation may provide protection to the photoreceptors by stimulating the selective expression of FGF-2 in the RCS rat (Ciavatta et al., 2006). While these studies show promise for subretinal electrical stimulation as a treatment of RP, implantation of MPA devices in S334ter rats does not preserve photoreceptors (Walker et al., 2005). We hypothesize that this may be due to the underlying mutations between RCS and S334ter rats. RCS rats have a recessive mutation in a tyrosine kinase gene, Mertk, which results in failed phagocytosis of shed outer segments by the retinal pigment epithelium (Mullen and LaVail, 1976; D’Cruz et al., 2000) while S334ter rats have a rhodopsin mutation which leads to photoreceptor death (Lee et al., 2003).

Rat models with photoreceptor degeneration are few while there are numerous mouse models of RP that have been described (Chang et al., 2002; Dalke and...
Thus, to further elucidate whether the neuroprotective effect of subretinal electrical stimulation is generalized to all types of photoreceptor degeneration, implantation of mouse models of RP would be advantageous. This study describes the development of surgical techniques and the success of implanting a small mouse eye with a subretinal MPA device.

2 Methods

2.1 Experimental and Implant Design

Adult wild-type C57Bl/6J mice (n = 6) were obtained from an in-house breeding colony originating from mice purchased from Jackson Laboratories (Bar Harbor, ME). Mice were implanted at 21–28 days of age and retinal function was measured every two weeks until 8 weeks post-implantation. After the final measurement, mice were euthanized and the eyes enucleated for histological assessment. All procedures were approved by the local Institutional Animal Care and Use Committee and carried out in accordance with the Association for Research in Vision and Ophthalmology statement concerning the use of animals in ophthalmic and vision research.

The MPA device was identical in electrical properties to devices described previously (Chow et al., 2001). Briefly, each device consisted of a silicon disk covered on the top side with a microphotodiode array. However, the devices were manufactured in a smaller size to accommodate the small mouse eye, measuring 23 μm thick and 0.5 mm in diameter.

2.2 Surgical Procedures

Surgical procedures were similar to that described for the rat eye (Ball et al., 2001). After dilation of the pupils (1% mydriacyl, 2.5% phenylephrine) and anaesthesia of the cornea (0.5% tetracine HCl), the anaesthetized (ketamine 80 mg/kg; xylazine 16 mg/kg) mouse was placed on a heating pad. A traction suture (8-0) placed in the superior lid was used to retract the upper lid while a second traction suture placed in the superior limbus was used to rotate the eye inferiorly (Fig. 1). The conjunctiva and underlying tenon capsule were opened using iris spring scissors to reveal the superior limbus. The tip of a 16 gauge stiletto blade was used to make a 0.6 mm long incision through the sclera, choroids, RPE, and retina, about 1 mm posterior to the limbus (Fig. 1). The eye was wet with saline (0.9% NaCl) and the retina was allowed to detach naturally along the incision over a period of 10 minutes, after which the implant was gently manipulated into the subretinal space using the tips of two IOL manipulators. The eye was then rotated back to primary position and the fundus was examined to confirm subretinal placement of the device. A drop of antibiotic solution was applied to the eye (Neosporin Ophthalmic Solution) and