1. INTRODUCTION

The mammalian retina has been a good model to investigate the central nervous system development. Among the five major types of mammalian retina, bipolar cells are known to develop relatively late, e.g. several days after birth in mouse (Wong, 2003; Morgan et al., 2006). Bipolar cells are important interneurons responsible for transmitting light signal from photoreceptors in the outer retina to ganglion cells in the inner retina via the ON/OFF pathways (Famiglietti and Kolb, 1976). The ON bipolar cells are depolarized to light onset, and ramify their axons in the inner portion of the inner plexiform layer (IPL), whereas the OFF bipolar cells are depolarized to light offset, and ramify their axons in the outer portion of the IPL. The precise ON/OFF segregation of bipolar cells during retinal development thus ensures correct visual signal transmission to the brain.

Throughout the retinal development, both intrinsic and extrinsic cues are important for the circuit maturation (Sernagor and Grzywacz, 1996; Wang et al., 2001; Kay et al., 2004). Experiments in some vertebrate species have demonstrated that spontaneous activities of developing ganglion cells and visual experience play significant roles on retinal network development (Tian and Copenhagen, 2001; 2003 ; Zhou, 2001) However, the mechanisms underlying the precise ON/OFF segregation of bipolar cells are largely unknown. Ablation of the ganglion cells in mouse at birth

did not disturb stratifications of bipolar cell axons in the IPL (Gunhan-Agar et al., 2000), and depletion of cholinergic amacrine cells at birth also did not alter the segregation of the projections of ON/OFF bipolar cells in the IPL (Gunhan et al., 2002). Furthermore, blocking AII amacrine cells during development has no significant effect on the axonal ramification of rod bipolar cells (Rice et al., 2001). Taken together, these evidences indicate that bipolar cell development is not sensitive to perturbation of inner retinal neurons. On the other hand, it has been reported that intraocular injection of the glutamate analog 2-amino-4-phosphonobutyrate (APB) at birth affects the stratification patterns of cat retinal ganglion cells (Bodnarenko and Chalupa, 1993). This result is commonly interpreted as glutamate-mediated afferent activity regulates the formation of ON and OFF pathways. It is possible that light deprivation may have altered this glutamate-mediated afferent activity not only on ganglion cell development but also on bipolar cell development. Recent evidence showed that rod bipolar cells correctly connect to cone photoreceptors even when rod photoreceptors were genetically knockout, and these rod bipolar cells have developed normal morphology (Strettoi et al., 2004). However, these mutant mice are still capable of detecting light through cone photoreceptors, leaving this glutamate-mediated afferent activity possible for bipolar cell development.

In this study, we specifically tested whether light deprivation at birth will affect

bipolar cell axonal stratification in rabbit retinas. Using gene gun technique and dye injection, we could label bipolar cells at different postnatal stages for normal-reared and dark-reared rabbits. To our surprise, we found that light deprivation causes a delay rather than a permanent arrest of the bipolar cell maturation.