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Influence of vitamin A on the regeneration of eye from damaged retinal pigmented epithelium cells in tadpoles of the toad, *Bufo melanostictus*

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In the present study complete eye was found to regenerate from a small part of retinal PECs in external gill stage tadpoles of *Bufo melanostictus*. More than half of the eye balls (including lens) were removed keeping a small part of neural retina intact in 40 tadpoles of external gill stage. Half (20) of the operated tadpoles were reared in tap water which served as control and remaining half (20) were reared in vitamin A (15 IU/ml) solution for five days and then transferred to water upto the day of termination of experiment (10th day after operation). Differences in retinal differentiation and the appearance of the new lens were noted between the two groups of tadpole. Although regeneration of eye was found in the both untreated as well as vitamin A treated tadpoles. However, vitamin A increased the percentage of eye regeneration. In the tadpoles of control group eye regeneration occurred only in 4 (20%) out of 20 whereas, it was in 16 (80%) out of 20 tadpoles of vitamin A treated group of the same age. Morphological and histological study revealed that newly regenerated complete eyes were similar to that of normal functional eyes.Similar experiment was performed on mature tadpoles of 5-toe stage. Vitamin A could induce eye regeneration in 12 (60%) out of 20 but regenerated eyes were found smaller in size. However, eye regeneration was not reported even in a single operated 5-toe stage tadpoles of untreated control group. This experimental model is the first to show that vitamin A can induce the developmental potency of neural retinal pigmented epithelial cells to regenerate not only the lost retinal cells but also the complete eye. Thus the results provide the basis for a new hypothesis concerning cytodifferentiation.

Key words: Complete eye regeneration, Vitamin A.

INTRODUCTION

REGENERATION is the ability of the fully developed organism to replace lost part/parts of the body by growth or remodeling of somatic tissues. It is a developmental phenomenon occurring during post embryonic period in an already formed and functional organism. One way or another, all animals possess the ability to regenerate damaged tissues. The degree of regeneration, however, varies considerably among tissues within a body and among species. Among vertebrates, amphibians have the ability to replace tails, limbs, a complete eye lens and a large portion of the retina from remaining pigmented epithelium.

(Niazi *et al* 1979, 1989; Niazi 1983; Jangir *et al* 1978,; Eguchi 1988, 1997; Reyer 1977, Okada 2000). However, examples of animals with the capacity for replacement of an entire eye are extremely limited (Rose 1964).

The analysis of eye tissue regeneration has been an important subject in developmental biology. Among the invertebrates, Eakin and Ferlatte (1973) found that Garden snail (*Helix aspersa*) had the ability to regenerate complete functional eye. The process of regeneration occurred through the mid-eye stalk and began by an invagination of integumentary epithelium at the apex of the stalk stump to produce a shallow cleft or "eye cup". Differentiation of all components of the eye occurred by transdifferentiation of these epithelial cells. Bever and Borgens (1988) also reported the ability to regenerate the eye completely after amputation through the mid eye stalk in the mystery snail. Eye regeneration in snail shares interesting similarities to the well studied regeneration of amphibian limbs, that is dependent on the intact nerve supply (Eakin and Ferlatte,1973;Bever and Borgens,1967,1988).

In the newt and some other limited animal species, the lens and neural retina can be regenerated completely through trans-differentiation of pigmented epithelial cells (PECs). Such a phenomenon, trans-differentiation, as observed in regeneration of ocular tissues seems to be highly powerful model for studying stability and instability in differentiation of tissue cells. The pigmented epithelium of vertebrate eyes is found to be most suitable tissue for such studies. Several workers reported retina regeneration from pigmented epithelium (Hasegawa 1958; Mitashov 1968, 69; Reyer 1971; Lopashov and Sologub 1972). It is reported that the removal of retina and iris in tadpoles of *Bufo viridis,* pigmented epithelium is not usually transformed into retina, but if it comes to lie between the margins of regenerating retina it is transformed into retina and lens as well (Lopashov 1949). Following the removal of retina in 4 day chick embryo it is not restored from the pigmented epithelium, but if a piece of retina from a chick embryo or a mouse embryo of the same age is transplanted into the cavity of such an eye, islets of retina arise in the pigmented epithelium (Coulumbre and Coulumbre, 1965, 1970). Lopashov and Sologub (1972) suggested that some retinal agent is essential for the trans-differentiation of pigmented epithelium cells into retina.

The capability of iris and retinal pigmented epithelial cells to transdifferentiate into lens is well documented in amphibians (Reyer, 1954, 1977; Eguchi & Itoh 1982; Eguchi 1988, 1997). However, this capability of iris and PECs is not restricted to amphibians only but widely conserved in almost all vertebrates (Eguchi 1997, Okada 2000). From this view point, trans-differentiation of PECs of vertebrates have revealed that dormant potential to transdifferetiate into retina and lens cells is widely conserved throughout vertebrate species and that cell type-specific genes are completely inactivated in the multipotent dedifferentiated cells originated from pigmented epithelial cells. Any factor that activates these specific genes may result the regeneration of complete eye.

Vitamin A is found to be an interesting model for its influence on such a transdifferentiation changes of one cell type to another. Excess of this vitamin A had been reported to destabilize cell membrane, stimulate synthesis and release of lysosomal

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