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***Review Article***

# SOMATIC DIFFERENTIATED CELLS CAN BE REPROGRAMMED-OVERVIEW

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## ABSTRACT
In this article, reprogramming ability of differentiated somatic cells under changed/ experimental conditions was reviewed. Experiments were performed on transdifferentiation of ocular tissue and tail tissue of toad tadpoles. Vitamin A was found to be a good model to enhance the reprogramming ability of tissue taken. Results report that vitamin A accelerated transdifferentiation of meshed ocular tissue explant into lens, retina and complete eye at injured site of tadpole's tail. Vitamin A also modifies the fate of injured tail tissue to transform into limb elements.

## INTRODUCTION
The prevalent view was that the mature cells were permanently locked into the differentiated state and unable to return to a fully immature pluripotent stem cell state. Gurdon (1962) revealed that a differentiated cell nucleus has the capacity to successfully revert to an undifferentiated state, with a potential to restart development. However, an open question remained, namely, whether it would be possible to induce reversion of an intact differentiated cell to a highly immature state? Many scientists considered this is impossible, or at the very least, that it would require very complex reorganization in the cell to unlock the differentiated state.

Nobel Laurates, Martin and Evans (2007) identified and characterized pluripotent embryonic stem cells. Whereas recently Gurdon and Yamanaka (2012) awarded Nobel Prize for their discovery that mature, differentiated cells can be reprogrammed to a pluripotent stem cell state. This represents a paradigm shift in understanding of cellular differentiation and plasticity of the differentiated state. Cellular differentiation appears as a unidirectional process, where undifferentiated cells mature to various specialized cell fates.

During normal development, cells proceed from the initial undifferentiated state of the egg and cells in the early embryo to a more specialized state. In the adult organism a range of differentiated cells are required to execute the specialized functions performed in the adult body. Thus during developmental journey, cells from totipotent condition (Zygote) become pluripotent (inner cell mass- can give rise to all somatic cells as well as to germ cell lineage)and then progressively cells become more restricted in their differentiation potential and as a consequence they do not retain pluripotency. Most cells mature into fully differentiated cells. Differentiated cells are remarkably stable and as a rule they will not shift fate into other types of differentiated cells or revert to the type of undifferentiated cells that can be found in the early embryo. For this reason, the long-standing predominant view was that cells in the somatic lineage were permanently in a locked state such that the journey back a highly undifferentiated state was impossible. Despite the dogma, the notion that specialized cells could somehow be unlocked from their differentiated state and dedifferentiation was not entirely dismissed.

A direct attempt to test whether differentiated cells in the somatic cell lineage were endowed with a dormant dedifferentiation potential was a first carried out by Brigs and King (1952) who developed a technology for transfer of somatic cells nuclei from undifferentiated and differentiated cells to an enucleated fertilized egg in the amphibian *Rana pipiens*. In a key study, Gurdon (1962) enucleated eggs by ultra violet irradiation and found that when the eggs were transplanted with nuclei from differentiated tadpole intestinal epithelium, a small number of swimming tadpoles were generated. Thus he concluded that differentiated somatic cells nuclei had the potential to revert to pluripotency. Later on a new research

field of centered on somatic cell nuclear transfer (SCNT) as a method to understand reprogramming and how cells change as they become specialized. In 1997, the first cloned mammal, the sheep Dolly, was born after SCNT from an adult mammary epithelial cell into an enucleated sheep egg (Wilmut *et al.,* 1997). Gurdon (1962) revealed that a differentiated cell nucleus has the capacity to successfully revert to an undifferentiated state, with a potential to restart development. Takahashi and Yamanaka (2006) identified some transcription factors as candidates to reinstate pluripotency in somatic cells. The pluripotent stem cells so obtained were called induced pluripotent stem cells (iPS cells).This was truly fundamental discovery, as it was the first time an intact differentiated somatic cell could be reprogrammed to become pluripotent. Experiments on plasticity and transdifferentiation are now a days in lime light and exercised in several field of medicine biology. For example, exocrine cells convert to endocrine cells in the pancreas by introduction of transcription factors (Zhou *et al* 2008). Similarly cadiomyocytes can be generated from fibroblasts *in vitro* and *in vivo* by introducing different transcription factors (Takahashi *et al.,* 2003, 2007; Chambers *et al.,* 2003; Ieda *et al.,* 2010; Song *et al.,* 2012; Qian *et al., 2012*).

Ocular tissues present a highly powerful model for studying plasticity in differentiation of tissue cells. In culture medium, it has been studied that the dormant potential of pigmented epithelial cells to transdifferentiate into lens is widely conserved in various animals including humans. This means that committed transient amplifying differentiating cells of another cell lineage. In *Xenopus laevis* lentectomy followed by regeneration of new lens from cornea (Freeman, 1963; Filoni, 1997; Bosco, 1988) while in some other amphibians, lens regeneration occurs by the dedifferentiation of pigmented epithelial cells of dorsal iris (Sharma *et al.,* 2010; Tsonis, 2004). This gives evidence of plasticity and reprogrammed fate of terminally differentiated tissue.

Lens regeneration in some of the amphibians from pigmented epithelial cells is one of the most spectacular cases of transdifferentiation of a terminally differentiated cell type to another (Jangir *et al.,* 2012, 2013; Tsonis *et al.,* 2000). Vitamin A and its derivatives retinoids, have remarkable effects on different systems in the developing embryo. Eyes are the organ whose development is largely dependent on retinoids and their receptors. Exogenous retinoic acid has been implicated in the induction of ectopic lens differentiation during eye development. Jangir *et al.,* (2012, 2013) found that somatic differentiated cells can change their fate under the influence of Vitamin A and transdifferentiate into another cell lineage. Their findings gives clear evidence of plasticity and reprogramming ability of differentiated tissue at ectopic site under the influence of Vitamin A. Vitamin A accelerated transdifferentiation of meshed ocular tissue grafts into lens, retina and even complete eye at mid lateral position of injured tail. Another study of plasticity and reprogramming ability of terminally differentiated tissue was observed in toad tadpole's tail where Vitamin A modified the fate of injured tail tissue to form additional body segments like pelvic girdle elements and hind limbs.

The research findings of plasticity and reprogramming ability of terminally differentiated ocular somatic cells under changed environment (influence of vitamin A) are supported by findings of Noble laureates, John and Shinya (2012). They demonstrated that the usually stable differentiated state of tissue cells can be unlocked because it harbors a potential (master switch gene) alters their state of developmental commitment. Similar findings have also been observed that cardiomyocytes can be generated from fibroblasts *in vitro* by introducing different transcription factors (Ieda *et al.,* 2010; Song *et al.,* 2012; Qian *et al.,* 2012). Thus it is clear from the above findings that even somatic differentiated cells or adult stem cells are more versatile than previously thought. Stem cells, including induced pluripotent stem cells (iPS) can potentially be used to replace diseased or lost cells in degenerative disorders including Parkinson's disease and type 1 diabetes. Cell replacement therapy with iPS cells can allow autologous cell grafting that would be less prone to immune rejection. The present work has introduced fundamentally new research area and offers exciting new opportunities to implement new therapies designated to repair the degenerated organs and visual function when conventional treatments are not efficacious.

## CONCLUSION

From the present study it can be concluded that mature, differentiated somatic cells can be reprogrammed under changed experimental conditions. This study offers new insight for furthers detail findings for therapies designated to repair the degenerated tissue or organs**.**

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