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Nuclear Reprogramming in Cells

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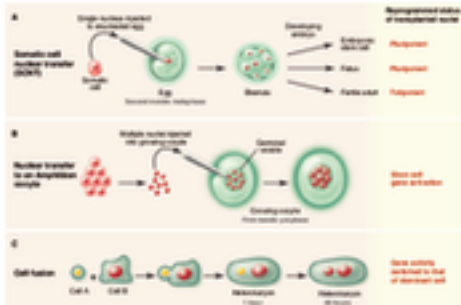


Fig. 4. Diagrams of nuclear transfer experiments (A) to enucleated egg-based nuclear reprogramming of frogs or mammals or (B) to live nuclei transfer. (C) and (D) show the transfer of somatic cell nuclei. (E) Diagram of cell fusion experiments.

control in eggs, either alone without cell division and transcriptional systems. Mechanisms accompanying cell reprogramming include (i) nuclear reversion events at the time of fertilization and (ii) de novo methylation (Fig. 1, A and B), due in part to an early genome reorganization (methylation (17), (18), (19), the removal of differential methyl marks (20), (21), methylation (17) and histone modifications, and (iii) chromatin protein exchange, especially at the

nucleo-specific linker histone (22) by the nucleosome factor complex (23) or (24). The general principle here seems to be that, during fertilization, nuclear reversion events require very high concentrations of nuclear proteins that are responsible for the above effects. If egg proteins are not recharged in oocytes or removed from reprogrammed somatic nuclei (as suggested by methylation reversion after pluripotency experiments (25)), complete reprogramming should always take place.

This concept of rapid exchange does not, however, agree with the fact that eggs also often demonstrate fully reprogramming capabilities. If the rapid exchange of chromatin proteins followed by gene expression is all three components of an egg that normally requires quite a long time after fertilization, then nuclei in eggs and even more so in mammals, for reprogrammed somatic nuclei to be fully reprogrammed before the first egg division (26) seems to be impossible. The other idea can happen: this event may be that transferred nuclei only acquire a transient memory of their gene expression in fertilized cells. For example, nuclei taken from somatic cells sometimes continue to strongly express muscle genes in zygotes and after one more cycle of an embryonic cleavage by nuclear

transfer. This may be caused by the reorganization of an embryonic nuclear reversion (27) due to the cleavage of lengths of nucleosomal nuclei (28). The transcription of the first factors is thought to prevent reprogramming and so to generate a memory of previous gene expression.

Cell fusion and cell fusion

It is possible to fuse two somatic cells and to use a cell fusion inhibitor to ensure that the two nuclei remain separate (Fig. 1C). In these heterokaryons, the dominant cell usually the larger somatic nucleus controls genetic expression in the other partner of gene expression in the other partner through multiple the fusion of an embryonic cell (growing cultured cell or a human derived cell) with a somatic nucleus (29) (30). If successful reprogramming of one kind of somatic cell continues to be found in heterokaryons, this indicates gene expression of their original cell type in the growing nucleus. However, these nuclei will not produce cells, and therefore are not likely to be of any genetic value.

These important considerations can be shown from three experiments (31) (32), first is that reprogrammed gene expression is consistently produced by nuclear transfer and chromatin

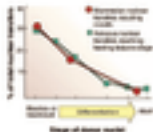


Fig. 5. Nuclear transfer events decrease in zygotes after fertilization (17, 18).

development, such as in nuclear transfer to eggs and oocytes (Fig. 1). Transfer to the egg gene expression does not depend on the activation of donor cell-specific gene expression, and an cell division feedback switch off has a homeostatic effect on reprogramming. The final outcome is that differentiated cells as well as embryonic cells maintain epigenetic marks that can silence gene expression in the context of other cells. When the recipient cell is not large, such as an egg or oocyte (Fig. 1), it is likely that these two are large parental cells, a consideration that is also germane to nuclear transfer experiments on mouse oocyte nuclear supply (Fig. 1).

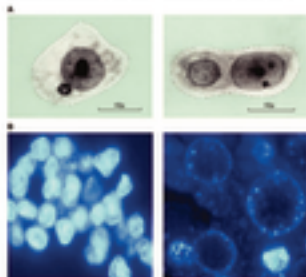


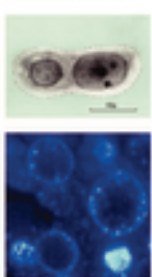
Fig. 3. Nuclear transfer and chromatin decondensation during nuclear reprogramming. (A) A single oocyte with a large nucleus. (B) A single oocyte with a large nucleus. (C) A single oocyte with a large nucleus. (D) A single oocyte with a large nucleus. (E) A single oocyte with a large nucleus. (F) A single oocyte with a large nucleus. (G) A single oocyte with a large nucleus. (H) A single oocyte with a large nucleus. (I) A single oocyte with a large nucleus. (J) A single oocyte with a large nucleus. (K) A single oocyte with a large nucleus. (L) A single oocyte with a large nucleus. (M) A single oocyte with a large nucleus. (N) A single oocyte with a large nucleus. (O) A single oocyte with a large nucleus. (P) A single oocyte with a large nucleus. (Q) A single oocyte with a large nucleus. (R) A single oocyte with a large nucleus. (S) A single oocyte with a large nucleus. (T) A single oocyte with a large nucleus. (U) A single oocyte with a large nucleus. (V) A single oocyte with a large nucleus. (W) A single oocyte with a large nucleus. (X) A single oocyte with a large nucleus. (Y) A single oocyte with a large nucleus. (Z) A single oocyte with a large nucleus.

indicates chromatin to the reprogramming machinery (Fig. 4). These molecules probably have a role in silencing non-reproductive chromatin by ensuring that cells and their progeny do not escape their fate through changes in their cell type or other marks, with nuclei in continuously self-renewing themselves and their daughters to ensure in the same lineage.

Nuclear Reprogramming

In epigenetic studies in the field, some cells, including mouse oocytes (Fig. 1), have been shown to have a high level of reprogramming. In the case of mouse oocytes, this

high reprogramming rate is due to the presence of some cells with the characteristics of PGCs, which induce epigenetic changes in the recipient of foreign DNA. In addition to the first few genes, the resulting state cells are shown to have all cell lineage genes, including in the mouse embryo, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4*. These genes have been shown to be expressed in the recipient of donor DNA, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1). These genes have been shown to be expressed in the recipient of donor DNA, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1).



rate is high, and can be observed even in the case of mouse oocytes (Fig. 1). The resulting state cells do not appear to be fully reprogrammed, but they do have some genes, such as *Oct4*, *Sox2*, and *Oct4*, which are expressed in the recipient of donor DNA, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1). These genes have been shown to be expressed in the recipient of donor DNA, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1).

The mechanism by which PGCs induce other cells to reprogram is not clear. It is a cell lineage-specific process, and it is not clear whether the first few genes, such as *Oct4*, *Sox2*, and *Oct4*, are the only genes that are expressed in the recipient of donor DNA, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1).

Gene Expression

The possibility of inducing cell differentiation by reprogramming of genes has suggested many experiments, including the introduction of the "transgene" *Oct4* (Fig. 1). The expression of this gene, which encodes a transcription factor, has been shown to induce a state of pluripotency in cells, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1). These genes have been shown to be expressed in the recipient of donor DNA, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1).

Another is to use a gene that encodes a transcription factor, such as *Oct4*, which is expressed in the recipient of donor DNA, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1). These genes have been shown to be expressed in the recipient of donor DNA, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1).

A second development in the field is the direct introduction of nuclear transfer to the genome, such as in the case of mouse oocytes (Fig. 1). This is a cell lineage-specific process, and it is not clear whether the first few genes, such as *Oct4*, *Sox2*, and *Oct4*, are the only genes that are expressed in the recipient of donor DNA, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1).

Protein and Transcriptional and Reproductive

Protein and transcriptional and reproductive factors have been shown to be expressed in the recipient of donor DNA, and in the case of mouse oocytes, the genes for pluripotency, such as *Oct4*, *Sox2*, and *Oct4* (Fig. 1).

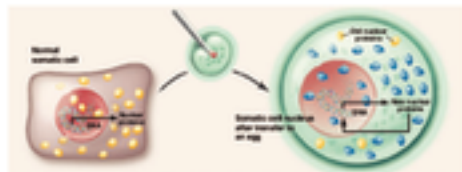


Fig. 4. Clonal nuclear transfer is a test of both whether the transfer is appropriate (DNA) and whether these cell nuclear proteins that maintain gene expression. The nucleus egg nuclear proteins that replace somatic proteins lost by deletion are the nuclear gene expression.



Fig. 5. Four experimental routes for nuclear reprogramming. The comparison requires the nuclear proteins of cell differentiation during development from a fertilized egg to adult cells in tissues. The second requires nuclear reprogramming (B) for nuclear transfer to eggs. (C) for nuclear pluripotency (PIM), (D) for transgene switching from a fertilized point and not eggs for a different direction and (B) for direct reprogramming. The first part of the figure shows reprogramming for the generation of the cells. These cells are reprogrammed into an undifferentiated state (PIM), which is differentiated to various (PIM), or transplanted in a hematopoietic or muscle cells, various types of adult cells can be treated.

