

Nuclear reprogramming—the experiment and mechanism

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To examine parameters characterize early development of nt-units derived from cross-species somatic cell nuclear transfer, we transplanted human fibroblasts into enucleated bovine oocytes (SCNT). Every nt-unit was photographed and subjected to DNA analysis. Data from such analyses indicated that a substantial percentage of the nt-units were activated and a proportion of them developed to the blastocyst stage. To address the question whether human genome can be activated by the cytoplasm of animal oocytes and to understand dynamics of such activation, we analyzed mRNA expression in nt-units at various pre-implantation stages. Results show that activation of human genes occurs randomly and is incomplete in most nt-units. Extent of human gene activation is closely correlated with developmental potential of the nt-units. Human gene activation takes place in 8- to 16-cell rather than 4- to 8-cell stages, therefore, follows the temporal order of the bovine, rather than the human.

In addition, we will present evidences to show that the maternal and paternal transcription profiles are reprogrammed to the zygotic equivalent using an “erase and rebuild” strategy. The same strategy is also used to reprogram somatic nuclei and duplicated maternal genome to the zygotic equivalent. Incomplete erasure of the existing somatic epigenetic program may account for high percentage of failures in SCNT experiments.

Keywords: SCNT, human, bovine, pre-implantation development, nuclear reprogramming

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