THE IMPROVED CULTURE CONDITION FOR MOUSE NUCLEAR TRANSFER EMBRYOS ENABLES HIGHLY EFFICIENT NUCLEAR REPROGRAMMING

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Somatic cell nuclear transfer (SCNT) offers a unique opportunity to produce cloned animals and to study reprogramming in oocytes. Growing evidence suggests that reprogramming of somatic nuclei in oocytes by means of SCNT results in embryonic stem cells of high quality, but the low success rate of SCNT remains an unsolved issue, warranting further investigation of this technology. Here, we find that the sequential supplementation of two small molecules after SCNT greatly improves cloning efficiency in mice and 15% of cloned embryos develop to term. We performed RNA-seq analysis using SCNT embryos at the 2 cell stage in order to examine the effect of small molecules on zygotic genome activation and identified genes that were upregulated upon treatment of the small molecules. Interestingly, expression of genes that were previously identified as resistant to reprogramming and of 2-cell-specific retroelements was upregulated. Moreover, the enhanced gene expression in SCNT embryos was associated with reduced histone H3 lysine 9 methylation, which has been shown to function as a major barrier for reprogramming. Thus our study indicates that the optimized culture condition with small molecules helps to overcome epigenetic barriers for reprogramming and ensues highly efficient development of SCNT embryos.