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Epigenetic Reprogramming and Cloning

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Although animal clones derived from somatic cells have been successfully generated in several mammalian species, there are still many unsolved problems in the present cloning technology. Somatic cell nuclear transfer has showed several developmental aberrancies including high abortion rate of early gestation and increased perinatal death. One cause of these developmental failures may be addressed in the epigenetic reprogramming of somatic donor genome. Epigenetic modification such as DNA methylation has been considered to be one of candidates regulating nuclear reprogramming. In mammals, DNA methylation is an essential process in the regulation of transcription during embryonic development and generally associated with gene silencing. A genome-wide demethylation may be a prerequisite for the formation of pluripotent stem cells that are important for the later development. We analyzed methylation patterns in cloned bovine embryos to monitor the epigenetic reprogramming process of donor genomic DNA. Aberrant methylation patterns were observed in various genomic regions of cloned embryos except single-copy sequences. The overall genomic methylation status of cloned embryos was quite different from that of normal embryos produced in vitro or in vivo, but it closely resembled that of donor cells. These results suggest that the developmental failures of cloned bovine embryos may be due to incomplete epigenetic reprogramming of donor genomic DNA. We also found a reverse relationship between methylation levels and inner cell mass versus trophectoderm ratios in cloned bovine blastocysts. Abnormal methylation profiles were specifically represented in trophectoderm cells of cloned embryos, which probably result in widespread gene dysregulation in extraembryonic region or placental dysfunction. In addition, a typical demethylation process observed in cloned porcine embryos implies that species-specific differences exist in modifying the epigenetic status of donor genome. More extensive studies on epigenetic reprogramming at the preimplantation stage will contribute to understand the molecular basis for developmental competence of cloned embryos.