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Epigenetic regulation and reprogramming: from embryos, to cloned embryos and to embryonic stem cells

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Preimplantation embryo development is marked with pronounced reprogramming of gene expression patterns during distinct transitions, namely the maternal-to-zygotic transition, compaction and blastocyst formation. Using microarray analysis, combined with functional genomics tools, we characterized global changes in gene expression and identified biological processes in mouse early embryo stages that accompany and likely underlie these transitions. For example, fertilization results in changes in the transcript profile in the 1-cell embryo that are far greater than previously recognized, and genome activation during 2-cell stage are quite selective rather than global and promiscuous, with genes involved in transcription and RNA processing being preferentially expressed. Nuclear transfer (NT) provides a useful model to further study the important reprogramming events in the early embryo, especially the maternal to zygote interrelationship. Since mitochondria (mt) are the most abundant maternally-inherited organelle, the effect of mtDNA haplotypes on bovine NT efficiency was evaluated. Our data suggests that mitochondrial structure, quantity and function may significantly affect the developmental competence of reconstructed embryos. As embryonic stem cells (ESCs) from cloned embryos would provide powerful research and clinical tools, we derived forty NT-ESC lines from NT embryos of different donor cell types or passages. These NT-ESCs expressed pluripotency stem cell markers in vitro and could differentiate into various embryonic tissues *in vitro* and *in vivo*. These studies of preimplantation embryo gene expression, epigenetic regulation, and their impact on ESC derivation provide a framework for understanding early development and stem cell biology.

Keywords: preimplantation embryo, expression profiling, nuclear transfer, mitochondria, embryonic stem cell

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