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Epigenetically unstable

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In the July 6 Science, Humpherys *et al.* describe extensive analysis of the expression of imprinted genes in mice derived from cloning by nuclear transfer (NT) (*Science* 2001, **293**:95-97). They examined mRNA levels for several imprinted genes including *H19* and *Igf2*, *Peg1/Mest*, *Mest/Grb10*, *Peg3* and *Snrpn*. They found that the expression of imprinted genes varied widely between the placentas of cloned embryos and in the organs of newborn cloned mice. *H19* expression was often silenced and *Igf2* expression was increased compared to controls. These abnormalities correlated with hypermethylation of the H19 differentially methylated region (DMR). Analysis of NT ES-cell clones and subclones revealed similar variations in *H19* and *Peg1* expression, differences in methylation and epigenetic heterogeneity. Humpherys *et al.* used tetraploid complementation and nuclear transfer experiments to show that the expression of imprinted genes varied widely even in mice derived from cells of the same ES-cell subclone. They conclude that the epigenetic state of ES cells is extremely unstable and that mammalian development appears surprisingly tolerant to epigenetic abnormalities.

References

1. *Science*, [http://www.sciencemag.org]

2. Hybrid vigor, fetal overgrowth, and viability of mice derived by nuclear cloning and tetraploid embryo complementation.

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