Not so fast: Differences in the first embryonic cell lineage decision of mammals

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New research shows that all not mammals are created equal. In fact, this work shows that the animals most commonly used by scientists to study mammalian genetics -- mice -- develop unusually quickly and may not always be representative of embryonic development in other mammals. The study, published by Cell Press in the February 14 issue of the journal *Developmental Cell*, identifies significant differences in the timing of cell fate commitment during mouse and cattle embryonic development and raises important strategic implications for the generation of embryonic stem cells.

The placenta in mammals is formed from cells called trophectoderm that arise from the very first lineage decision made by the early embryo. Most trophectoderm research is performed on mice, as other mammals tend to be much harder to work with in a lab. In the mouse, the fate of trophoectoderm cells is sealed (committed) by the mid-blastocyst stage. This fate commitment is driven in part by repression of the stem cell factor Oct4.

"We were intrigued by previous observations that in mammals such as humans, cattle, pigs and rabbits Oct4 protein was not shut down in the trophoectoderm of late blastocyst embryos," explains senior author Dr. Peter L. Pfeffer from AgResearch Crown Research Institute in Hamilton, New Zealand. Using cattle as a non-rodent model system, Dr. Pfeffer and colleagues discovered that cattle trophoectoderm cells were committed to their fate much later than mouse cells, with Oct4 expression levels remaining strong for longer than in mice. In fact the

authors identified the specific evolutionary changes in mouse DNA that make Oct4 behave differently in mice than in other mammals.

"Somewhat ironically, our studies in cattle led to new insight into Oct4 regulation in the mouse," explains Dr Pfeffer. "Such evolutionary differences in the regulation of the key stem cell gene Oct4 may explain the difficulty in embryonic stem cell derivation in mammals other than the mouse." Based on the fact that mouse embryos implant in the uterus at an earlier developmental stage than other mammals do, and therefore require earlier trophectoderm formation, the authors also speculate that the unusually rapid repression of Oct4 in mouse trophectoderm represented a key evolutionary step enabling early implantation.

"Establishing cattle as a second functional mammalian embryological model system challenges notions that mice are representative of either the earliest stages of mammalian development or of embryonic stem cell biology," concludes Dr. Pfeffer.

Provided by Cell Press