STEM CELLS

Human stem cells from cloned embryos

Methodological optimization makes possible the long-awaited derivation of human embryonic stem cells from embryos obtained with somatic cell nuclear transfer.

In several species, transfer of a somatic cell nucleus into the cytoplasm of an enucleated oocyte reprograms the somatic nucleus to a totipotent state. Embryonic stem cells (ESCs) can then be derived from the resulting blastocyst. In the human, however, this has not been successful until now. Embryos that result from human somatic cell nuclear transfer (SCNT) typically arrest early in development.

Shoukrat Mitalipov and colleagues at Oregon Health and Science University, who have previously described SCNT and ESC derivation with nonhuman primate cells, now report that they have achieved this feat with human cells as well. Perhaps unsurprisingly, the solution to the problem of arrested development in SCNT embryos came from methodological optimization coupled to knowledge of human oocyte biology.

Working first with monkey cells, the researchers optimized conditions for fusion of the donor cell to the enucleated oocyte (using a viral protein) as well as for activation of the resulting embryo. They determined the concentrations and exposure times of the histone deacetylase inhibitor trichostatin A that yield optimal development of the SCNT embryo to the blastocyst stage.

Applying these methods successfully to human cells required a step further. Human SCNT embryos under the optimized conditions developed to the blastocyst stage at some frequency but did not yield stable ESCs.

On the basis of their own and others' observations, the researchers reasoned that the problem might lie in the propensity of human oocytes to emerge prematurely from meiotic arrest upon enucleation and spindle removal, which could degrade their reprogramming ability. They therefore exposed the oocytes to caffeine, which is known to protect the enucleated oocyte from premature activation. This, they report, did the trick! A dose of caffeine during spindle removal and donor cell fusion made it possible to derive stable ESC lines from embryos generated in three independent SCNTs from six human donors.

Though marred slightly by reports of errors and mislabeling in the published paper—a disturbing occurrence considering the tarnished history of this field—this much-awaited achievement now opens the door to tailored (person- or disease-specific) human cells derived from embryonic stem cells. The field eagerly awaits tests of the robustness of these methods in other labs.

Natalie de Souza

RESEARCH PAPERS

Tachibana, M. *et al.* Human embryonic stem cells derived by somatic cell nuclear transfer. *Cell* **153**, 1228–1238 (2013).