Expanded Potential Stem Cells: A New Tool for Basic and Translational Research

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By inhibiting signal pathways implicated in the earliest embryo development, we established cultures of mouse expanded potential stem cells (EPSCs) from individual 4-cell and 8-cell blastomeres, by direct conversion of embryonic stem cells (ESCs) and through reprogramming somatic cells. A single EPSC can contribute to both the embryo proper and the TE lineages in chimera assay. *Bona fide* trophoblast stem cell (TSC) lines, extra-embryonic endoderm stem (XEN) cells, and ESCs could be directly derived from EPSCs *in vitro*. Molecular analyses of the epigenome and single-cell transcriptome reveal that EPSCs have enriched features of cleavage stage embryos. The knowledge of mouse EPSCs has enabled the establishment of EPSCs of human, pig, bovine and additional mammalian species. EPSCs of these species share similar molecular features and have the potential to differentiate to extra-embryonic as well as embryonic cell lineages *in vitro* and in chimeras (animal EPSCs). They are genetically and epigenetically stable, can be maintained in homogenous long-term cultures and permit efficient precision genome editing. EPSCs thus provide new tools for studying normal development and open up new avenues for translational research in biotechnology, agriculture, and regenerative medicine. For example, we find that early syncytiotrophoblasts generated from human TSCs are highly susceptible to coronavirus infection and are sensitive to antiviral treatment. These findings may facilitate stem cell-based antiviral drug discovery. I will discuss our thoughts on collaborations with colleagues in various research areas.

Key words: EPSCs, pluripotency, totipotency, antiviral, development, epigenome