Derivation of stem cells with totipotent features in mice and humans

Subject Code: C07

With the support of the National Natural Science Foundation of China, a research group led by Prof. Deng Hongkui (**邓宏魁**) from Peking University, in collaboration with researchers from the Salk Institute and Peking University People's Hospital, demonstrates that the developmental potentials of stem cell lines could be expanded to both embryonic and extraembryonic lineages in mice and humans using a chemical cocktail (*Cell*, 2017, 169: 243—257).

During development, both the zygotes and blastomeres are regarded as totipotent cells, which can give rise to all embryonic and extra-embryonic lineages. However, establishing stem cell lines with such developmental potential has been a major challenge in stem cell biology.

In this study, through chemical screening, we identified a chemical cocktail (LCDM condition) that enables the generation and long-term propagation of stem cell lines with both Em and ExEm differentiation potentials. These cells are termed as extended pluripotent stem (EPS) cells. The developmental potency of EPS cells was demonstrated at the single-cell level. Remarkably, a single mouse EPS cell shows widespread chimeric contribution to both embryonic and extraembryonic lineages *in vivo* and permits generating single-EPS-cell-derived mice by tetraploid complementation. In addition, human EPS cells show robust interspecies chimeric competency in mouse conceptuses, the efficiency of which is approximately 20 folds higher than that using human naïve pluripotent cells in previous studies.

This study demonstrates the feasibility of generating stable stem cell lines with both embryonic and extraembryonic developmental potency. EPS cell lines provide a useful cellular tool for gaining a better molecular understanding of initial cell fate commitments and generating new animal models to investigate individual development. Furthermore, they also provide an unlimited cell resource and hold great potential for *in vivo* disease modeling, *in vivo* drug discovery, and *in vivo* tissue generation in the future. Finally, this study opens a path toward capturing stem cells with intra- and/or inter-species bi-potent chimeric competency from a variety of other mammalian species.

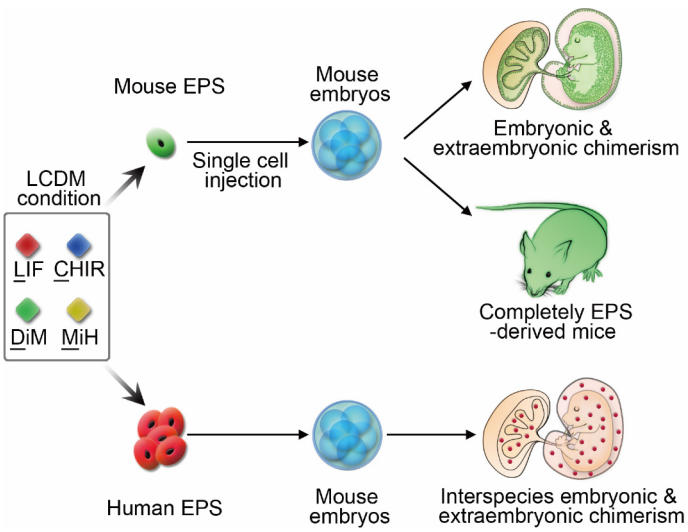

Figure Derivation of EPS cells with embryonic and extraembryonic developmental potency.