

Formative pluripotency and in vitro germ cell derivation for disease modeling

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Abstract

Different formative pluripotent stem cells are recently established harboring similar functional properties of lineage neutral and germline competence yet with distinct molecular identities. Here, we show that WNT/ β -catenin signaling activation can sustain transient mouse epiblast-like cells as epiblast-like stem cells (EpiLSCs). EpiLSCs display metastable formative pluripotency with bivalent cellular energy metabolism and unique transcriptomic features and chromatin accessibility. We develop scSTALT to study formative pluripotency continuum and revealed that EpiLSCs recapitulate a unique developmental period in vivo and fill the gap of formative pluripotency continuum between other published formative stem cells. WNT/ β -catenin signaling activation counteracts differentiation effects of Activin A and bFGF by preventing complete dissolution of naïve pluripotency regulatory network. Moreover, EpiLSCs have direct competence for the germline specification, which is further matured by supplement of FGF receptor inhibitor. Our EpiLSCs can serve as a unique in vitro model for mimicking and studying early post-implantation development and pluripotency transition.

Biography

Qiaolin Deng obtained her Ph.D degree in developmental biology and stem cell biology at Karolinska Institutet in 2010 and discovered the pivotal role of transcription factor Lmx1a in dopamine neuron specification published in Cell. From 2011-2014, she received the postdoctoral fellowship from Swedish national medical research council and joined Prof. Rickard Sandberg's lab at Ludwig Institute of Cancer Research involving in inventing Smart-seq & Smart-seq2 single-cell RNA-seq technology. Her postdoctoral work pioneered in single-cell analysis of preimplantation development in mouse and human and firstly described random allelic gene expression due to stochastic transcription, published in Science and Cell.

From 2015, Qiaolin established her independent research group and currently holds the Associate Professor position at Dept. Physiology and Pharmacology, Karolinska Institutet and is affiliated to Center for Molecular Medicine at Karolinska University Hospital. Her research is focused on understanding gene regulation of cell fate specification, pluripotency transition as well as dynamics of X-chromosome activity. Her lab also further developed single-cell sequencing, i.e. LCM-seq for spatially profiling of neurons in postmortem human tissue. Her lab also applies single-cell sequencing in characterizing molecular signature at disease condition including polycystic ovary syndrome (PCOS), wound healing and diabetes. These work has been published in Nature Medicine, Nature Communications, and Cell Reports etc. Her lab is mainly funded by prestigious grants from Swedish Society for Medical Research, Swedish Medical Research Council, Wallenberg Foundation in Medicine among others. Besides, Qiaolin has also served as the grant reviewer in research council of several countries including Sweden, the Netherlands, UK and Israel as well as European Research Council.

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All are welcome!