

Department of Systems Medicine Presents

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場所: 信濃町キャンパス
総合医科学研究棟5F 会議室

参加自由

Derivation and Expansion of Naïve Pluripotent Stem Cells in Suspension Bioreactor

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Bioreactors permit pluripotent stem cell (PSC) scale up in a controlled culture environment. We have observed that aggregates of murine (m) PSCs experience “mechano-pluripotency” in suspension bioreactors: fluid shear manifested at adherent junctions (AJs) results in the nuclear translocation of β -catenin and upregulation of pluripotency related genes in the absence of LIF. By contrast, conventional human (h) PSCs do not undergo mechanopluripotency because ROCK inhibitor (Y-27632) is necessary to stabilize AJs in the bioreactor. However naïve hPSCs, which do not require Y-27632 for passaging, may undergo mechanopluripotency like their mPSC counterpart. Recently we investigated if naïve hPSCs could be derived and expanded without requiring Y-27632. H9 cells were reverted to the naïve state in bioreactors. Resulting aggregates could be passaged several times without Y-27632 and revealed domed shaped colonies in static culture. Naïve aggregates expressed high levels of naïve pluripotency markers and concomitant disappearance of XIST gene expression. Furthermore, naïve aggregates showed bivalent function like their mPSC counterpart and could convert between mitochondrial and glycolytic metabolism depending on their culture conditions. Our research suggests that the reversion to naïve pluripotency in bioreactors may be a viable approach to generate the large numbers of hPSCs required for future clinical application. Given the negative effects that Y-27632 has on hPSCs, our approach may ensure the clinical use of legacy hPSCs.

* セミナーは英語で行います。

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