446th IMEG Seminar

【Date】Feb 6 (Mon), 2023　13:00～14:00

【Venue】On-line Zoom (The Zoom ID and passcode were sent via email.)

【 Title 】"Molecular mechanism underlying the heterogeneity of mouse embryonic stem cells"

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【Abstract】

Naïve pluripotency is characteristic of early epiblast in pre-implantation mouse blastocysts and its *in vitro* counterpart embryonic stem cells (ESCs). The pluripotency is maintained in the serum and Leukemia Inhibitory Factor (LIF) culture condition, and under the condition, ESCs manifests the heterogeneity of naïve marker genes including *Nanog, Rex1, Klf4*, and *Stella*. While naïve marker-positive and negative ESCs are converted into each other's state, naïve marker-positive ESCs, but not negative ESCs, contribute to chimaera formation. Molecular mechanism generating the heterogeneity is considered to be governed by phosphorylated ERK (pERK) and the pERK is mainly brought by Fgf4 and its receptors.

We find that pERK level is higher in Rex1/Nanog-positive ESCs than in Rex1/Nanog-negative ESCs and by using a Fgf inhibitor, pERK level and the heterogeneity in ESCs is determined in part by Fgf signaling. We show that *Lifr* and *gp130* are abundantly expressed in Rex1 and Nanog-positive ESCs, and a gp130 mutant ESCs which is defective for ERK activation upon LIF binding exhibit highly homogenous Nanog expression. The scRNA-seq and cap analysis gene expression clearly demonstrated that the gp130 mutant ESCs are close to Nanog-positive ESCs at transcription, promoter and enhancer levels. Together, our data indicate that the heterogeneity of ESCs significantly attributes to LIFR-gp130-pERK axis.

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