第 469 回つくば分子生命科学セミナー

TSUKUBA MOLECULAR LIFE SCIENCE SEMINAR

演題：Distinct phospho-variants of STAT3 regulate developmental pace *in vivo.*

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日時：2022 年 12 月 15 日（木）　17:00-18:30

会場：医学系棟 483 室

要旨：

STAT3 has been studied extensively in the context of self-renewal of naïve pluripotent mouse embryonic stem cells (mESCs). Although STAT3 is required to maintain ICM lineages when maternally eliminated, the role of STAT3 during gastrulation is unclear as the conventional knockout of Stat3 develops until E6.5. In this study, we observed that zygotic loss of Stat3 on CD1 genetic background leads to consistent developmental retardation from implantation to mid-gestation, beginning with a significant reduction in the number of epiblast cells by the time of implantation. Remarkably, mutants appear to scale normally and resemble non-affected embryos from the previous day at all postimplantation stages examined. We attribute this phenotype to loss of the active serine phosphorylated (pS727) form of STAT3, required for neural differentiation of mESCs, which is also implicated in growth defects during organ expansion in mice and humans. We demonstrate that gastruloids, an *in vitro* model for the gastrulating stage embryos, from Stat3 null ESCs failed to extend the posterior axis and maintain Brachyury expression. Furthermore, we have established mutations associated with human undergrowth syndromes into our human embryonic stem cells. Our study demonstrates the role of the STAT3 in the temporal control of embryonic progression and metabolic mechanisms.

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