



第5回若手セミナー

筑波大学 テニュアトラック普及・定着事業
(共催：第361回つくば分子生命科学セミナー)

演題：Orphan Nuclear Receptors $ERR\alpha/\gamma$ Are Competence Factors For Somatic Cell Reprogramming

演者：木田 泰之 先生

産業技術総合研究所 幹細胞工学研究センター
間葉系幹細胞ダイナミクス研究チーム長

日時：2012年11月30日(金) 17:00-18:30

会場：医学系棟4階482室

要旨：While cell metabolism is adaptive to extrinsic demands, little is known about metabolic alterations required for the unique intrinsic demands associated with induced pluripotent stem cell (iPSC) reprogramming. This study identifies characteristic temporal expression patterns for the nuclear receptor family of transcription factors during iPSC generation in adipose derived stem cells (ADSCs) and embryonic fibroblasts (human and mouse) that correlate with developmental transitions in the cell. Bioenergetic assays demonstrated that while glycolysis increases throughout the reprogramming transition, an early and transient OXPHOS burst is required for pluripotency initiation and progression. This OXPHOS burst coincides with a robust but transient induction of Estrogen-related receptor α or γ ($ERR\alpha$ or γ) and the co-activators $PGC-1\alpha$ and β in human and mouse cells. We demonstrate that an ERR isoform is enriched in sub-population of cells that successfully, highly efficiency, undergo reprogramming, and is required for the metabolic transition of the iPSC reprogramming event. Furthermore, abrogation of ERR expression results in a complete collapse of the regeneration program. The existence of an ERR-dependent checkpoint reveals a new critical step in somatic reprogramming and raises questions as to how metabolic switching enables pluripotency and whether ERR ligands can be used to manipulate the process.

REFERENCE:

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2. Sugii, et al. (2011) *Nat. Protoc.*, 6: 346-358.
3. Lister, et al. (2011) *Nature*, 471: 68-73.
4. Sugii, et al. (2010) *P.N.A.S.*, 107: 3558-3563.
5. 川村晃久, 木田泰之 (2012) *医学の歩み*, 242: 337-342.

連絡先：テニュアトラック普及・定着事業 医学医療系 西村 健 (内線 3929, ken-nishimura@md.tsukuba.ac.jp)
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