CDB SEMINAR

Knut Woltjen

CiRA, Kyoto University

Friday, March 29, 2013

16:00~17:00 A7F Seminar Room

Cell Identity Transitions During Induced Reprogramming to Pluripotency

Summary

Reprogramming of somatic cells to induced pluripotent stem cells (iPSCs) by transcription factor overexpression represents a paradigm where exogenous transcriptional activator/repressor proteins are implemented to elicit changes in gene expression, ultimately altering cell fates. Oct3/4, Sox2, cMyc, and Klf4 (the "Yamanaka factors") are capable of re-wiring a somatic cell to achieve pluripotency.

We have developed doxycycline (dox)-inducible, combinatorial transgene systems for reprogramming somatic cells, permitting observation of dynamic changes in response to fixed factor stoichiometries. We employed these composite systems in MEFs, uncovering a fundamental difference in one commonly used factor that leads to distinct cellular fates.

Differences in factor expression reproducibly manifest disparate effects on proliferation, morphology and colony formation, through differential modulation of the severity of the mesenchymal-epithelial transition (MET). Subsequent late-stage factor levels impact endogenous pluripotency gene expression and apparent iPSC quality. Our data implies discrete reprogramming factor requirements at each stage of the process, and prospective refinement of current reprogramming standards.

Host:
Hitoshi Niwa
Pluripotent Stem Cell Studies, CDB
niwa@cdb.riken.jp
Tel:078-306-1930 (ext:1461)