第 472 回 難研セミナー
第 45 回難治疾患共同研究拠点セミナー
Stem Cell Regulation Seminar

【日　時】　平成 24 年 6 月 11 日（月）15:00 ～ 16:00

DATE/TIME: **June 11th, 2012 (Monday) 15:00 - 16:00**

【場　所】　M&D タワー24 階 共用セミナー室 1

PLACE: **Common Seminar Room 1, M&D Tower, 24th Floor**

【演　題】Transcription factor interactions in ES cells

TITLE:

Transcription factor interactions in ES cells

【演　者】　Ian Chambers 教授（エジンバラ大学）

SPEAKER: **Dr. Ian Chambers, Professor of Pluripotent Stem Cell Biology, University of Edinburgh**

Prof. Chambers has been working on the mechanisms regulating pluripotency of embryonic stem (ES) cells. He is a discoverer of a homeodomain protein, Nanog, which maintains ES cell self-renewal in the absence of cytokine stimulation, conditions under which differentiation normally ensues.

Publications:

Chambers et al. (2003). Functional expression cloning of Nanog, a pluripotency sustaining factor in mouse embryonic stem cells. Cell 113: 643-655.

Chambers et al. (2007) Nanog safeguards pluripotency and mediates germ cell development. Nature, 450, 1230-1234.

Mullin et al. (2008) The pluripotency rheostat Nanog functions as a dimer. Biochem. J. , 411, 227-231

Silva et al. (2009) Nanog is the gateway to the pluripotent ground state. Cell, 138, 722-737.

van den Berg et al. (2010) An Oct4-centred protein interaction network in embryonic stem cells. Cell Stem Cell, 6, 369-381.

Navarro et al. (2010) Molecular coupling of Tsix regulation and pluripotency. Nature, 468, 457-460.

Osorno, R. et al. (2012) The developmental dismantling of pluripotency is reversed by ectopic Oct4 expression. In press at **Development.**

連絡先：　幹細胞制御分野　田賀哲也（内線 5814）
共　催：　発生再生生物学分野　仁科博史

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<Abstract>

Transcription factor interactions in ES cells

Ian Chambers

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We study pluripotent Embryonic Stem (ES) cells. Our goal is to define the mechanisms by which key regulatory molecules direct ES cell self-renewal and differentiation, with our principal focus on self-renewal. To achieve this it is important to (i) identify the molecules that direct self-renewal, (ii) determine the biological function of these molecules and (iii) define how these molecules interact at an atomic level to fulfil their function.

ES cells possess the paradoxical capabilities for both self-renewal and differentiation into derivative cells of all three primary germ layers. Indeed it is the simultaneous possession of these two properties that defines ES cells and makes them useful.

We cloned the pluripotent cell specific transcription factor Nanog using a genetic screen for enhanced self-renewal. As Nanog allows ES cells to self-renew under conditions in which they would normally differentiate, we named it after Tir nan Og, the mythological Celtic land of the ever-young.

We have found that undifferentiated ES cells are not all the same. Indeed undifferentiated ES cells fluctuate between states of high Nanog expression, associated with a high probability of self-renewal, and low Nanog, associated with a pre-disposition towards differentiation. Therefore loss of Nanog can be dissociated from commitment to differentiation. Rather than being essential for ES cell self-renewal, Nanog acts like a dimmer switch to modulate ES cell self-renewal efficiency

We are currently investigating the differences between ES cells that do or do not express Nanog and are particularly interested in the mechanisms by which cells switch between the two states. In addition, we are investigating the molecular relationship between ES cells and the developmentally more advanced pluripotent cells of the post implantation embryo and their in vitro derivatives, epiblast stem cells (EpiSCs).