



STEM CELL SOCIETY
SINGAPORE



Singapore
Stem Cell Consortium

STEM CELL CLUB

Co-hosting with Singapore Stem Cell Consortium, A*STAR
4.30pm - 5.30pm

Tuesday 19 October 2010 • Aspiration Theatre, Matrix Building Level 2M,
30 Biopolis Street, Singapore 138671

PROGRAMME

4.30 - 5.00pm

Dr. Krishanu Saha, PhD

Rudolf Jaenisch Laboratory, Whitehead Institute/MIT, Cambridge, MA USA

“Direct reprogramming of mammalian cells to pluripotent states”

5.00 - 5.30pm

Heng Jian Chien Dominic

Gene Regulation Laboratory, Genome Institute of Singapore

“Generation of induced pluripotent stem cells with nuclear receptors”

5.30pm onwards

Network Social

Provided by Stem Cell Society Singapore

Only for members of Stem Cell Society Singapore ; Non-members who wish to attend Network Social could sign up for membership at the seminar

Hosted by

Dr Alan Colman

Executive Director, Singapore Stem Cell Consortium

SPEAKER

Dr Krishanu Saha, PhD

Direct reprogramming of mammalian cells to pluripotent states

Abstract

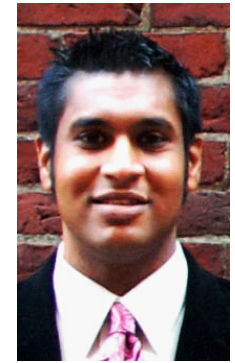
Currently, new cellular models of human disease are emerging through the use of reprogramming technology. Direct reprogramming of human somatic cells to embryonic-like induced pluripotent stem (iPS) cells uses readily accessible skin, fat, blood, and hair cells. A primary use of such technology is to reprogram somatic cells from patients who are classified into a disease group, thus creating iPS cell lines popularly labeled as “diseases in a dish.” To fully realize the potential of such reprogrammed cells, we need to understand the molecular and epigenetic determinants that convert one cell type into another, as well as the integration of this technology into emerging translational medicine efforts.

In this talk, I will describe our efforts to monitor and model the somatic to iPS cell transition quantitatively. We characterized the reprogramming efficiency and kinetics of over 1000 somatic cell derived monoclonal populations over an extended period of time. The process appears to be stochastic and inefficient,

with long timescales for rate-limiting processes to occur. We will also demonstrate that human somatic cells can be reprogrammed to distinct pluripotent states, corresponding to the inner cell mass and epiblast developmental stages. The induction of these pluripotent cell types was highly sensitive to the in vitro culture conditions during reprogramming. This work helps begin to define experimental conditions that allow the development and detection of relevant in vitro cellular phenotypes for a given human disease, putting “personalized” regenerative medicine, disease modeling, and translational medicine at the horizon.

Biography

Krishanu Saha studied Chemical Engineering at Cornell University and at the University of California in Berkeley. In his dissertation he worked on experimental and computational analyses of neural stem cell development, as well as the design of new materials for adult stem cell culture. In 2007 he became a postdoctoral fellow in the laboratory of

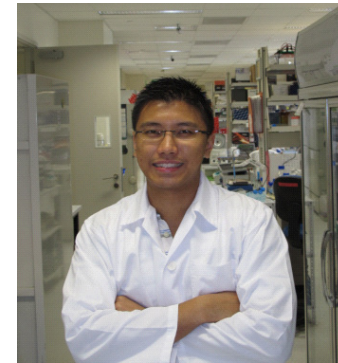


Professor Rudolf Jaenisch at the Whitehead Institute for Biomedical Research at MIT in Cambridge, Massachusetts. Concurrent with his laboratory research, he also works with Professor Sheila Jasanoff in the Program on Science, Technology and Society at the Kennedy School of Government at Harvard University. Since 2006 he has done research on human embryonic stem cells and the institutional policies surrounding them. As a Society in Science: Branco-Weiss Fellow, Kris is expanding his background in working with nascent human engineered materials to investigate the modeling of diseases at the cellular level with human “reprogrammed” stem cell lines.

SPEAKER

Heng Jian Chien Dominic

Generation of induced pluripotent stem cells with nuclear receptors



Abstract

In his groundbreaking discovery, Shinya Yamanaka demonstrated that induced pluripotent stem cells (iPSCs) can be generated via the introduction of transcription factors Oct4, Sox2, Klf4 and c-Myc. However, this transcription factor quartet is not the only combination of factors that can faithfully reprogram somatic cells to a state of pluripotency. James Thomson and colleagues reported a unique repertoire of factors that comprises Oct4, Sox2, Nanog and Lin28. In addition, other transcription factors such as Utf1 have been shown to enhance the efficiency of reprogramming. Prior to our studies, nuclear receptors, a class of transcription factors, have not been implicated in the reprogramming of somatic cells to iPSCs. Strikingly, we found that Esrrb, an orphan nuclear receptor can replace Klf4 in reprogramming. In addition, from a screen of several nuclear receptors, we found that Nr5a2 was not only able to enhance the generation of iPSCs but can also replace exogenous Oct4 in reprogramming. The replacement of Oct4 with Nr5a2 was indeed a remarkable discovery as no

other factors have been shown to be able to substitute for the exogenous introduction of Oct4. Similar to how close relatives of Sox2, Klf4 and c-Myc can substitute them in reprogramming, we show that close relatives of Esrrb and Nr5a2 can also replace their counterparts in reprogramming. Interestingly, we demonstrate that sumoylation site mutants of Nr5a2 can further enhance its reprogramming capacity. Taken together, our studies have uniquely highlighted the roles that nuclear receptors can play in reprogramming and that the reprogramming process can be largely initiated by various non-canonical transcription factors.

Biography

Dominic pursued an accelerated bachelors program at the School of Biological Sciences at Nanyang Technological University (NTU), and in 2008 graduated with a Bachelor of Science degree in which he was awarded a first class honors. He was then conferred a National University of Singapore graduate school for integrative sciences and engineering

(NGS) scholarship for his postgraduate studies. Dominic embarked on his PhD research which entails the study of various non-canonical transcription factors that could also participate in the generation of induced pluripotent stem cells in the laboratory of Dr Ng Huck Hui. In 2009, he was involved in a Nature Cell Biology publication that reported on the orphan nuclear receptor, Esrrb in the reprogramming of mouse fibroblasts. Early this year, he published his findings on the nuclear receptor Nr5a2 in reprogramming in Cell Stem Cell, a very high impact journal in the stem cell biology field. Recently he was not only conferred a travel award for the 2010 International society for stem cell research (ISSCR) conference but was also awarded the best poster award at this year's ISSCR meeting, which is one of most renowned stem cell conferences held annually.