CLINICAL EPIGENETICS

MEETING ABSTRACT Open Access

FGF signalling inhibition in ESCs drives rapid genome-wide demethylation to the epigenetic ground state of pluripotency

Gabriella Ficz[1], Timothy A Hore[1], Fatima Santos[1], Heather J Lee[1], Wendy Dean[1], Julia Arand[2], Felix Krueger[3], David Oxley[4], Yu-Lee Paul[1], Jörn Walter[2], Simon J Cook[5], Simon Andrews[3], Miguel R Branco[1,6], Wolf Reik[1,6,7*]

From Birminghm Cancer Epigenetics Conference; Translational Opportunities
Birmingham, UK. 16 May 2013

Genome-wide erasure of DNA methylation takes place in primordial germ cells (PGCs) and early embryos and is linked with pluripotency. Inhibition of Erk1/2 and Gsk3β signalling in mouse embryonic stem cells (ESCs) by small molecule inhibitors (called 2i) has recently been shown to induce hypomethylation. We show by whole-genome bisulphite sequencing that 2i induces rapid and genome-wide demethylation on a scale and pattern similar to that in migratory PGCs and early embryos. Major satellites, intracisternal A particles (IAPs) and imprinted genes remain relatively resistant to erasure. Demethylation involves oxidation of 5-methylcytosine (5mC) to 5-hydroxymethylcytosine (5hmC), impaired maintenance of 5mC and 5hmC and repression of the *de novo* methyltransferases (Dnmt3a, Dnmt3b) and Dnmt3L. We identify a Prdm14 and Nanog binding *cis*-acting regulatory region in *Dnmt3b* that is highly responsive to signalling. These insights provide a novel framework for understanding how signalling pathways regulate reprogramming to an epigenetic ground state of pluripotency.

doi:10.1186/1868-7083-5-S1-S2
Cite this article as: Ficz *et al.*: FGF signalling inhibition in ESCs drives rapid genome-wide demethylation to the epigenetic ground state of pluripotency. *Clinical Epigenetics* 2013 **5**(Suppl 1):S2.

Authors' details
[1]Epigenetics Programme, The Babraham Institute, Cambridge, CB22 3AT, UK. [2]Department of Biological Sciences, Institute of Genetics/Epigenetics, University of Saarland, Saarbrüken, Germany. [3]Bioinformatics Group, Babraham Institute, Cambridge CB22 3AT, UK. [4]Proteomics Research Group, Babraham Institute, Cambridge CB22 3AT, UK. [5]Signalling Programme, The Babraham Institute, Cambridge, CB22 3AT, UK. [6]Centre for Trophoblast Research, University of Cambridge, Cambridge CB2 3EG, UK. [7]Wellcome Trust Sanger Institute, Hinxton CB10 1SA, UK.

Published: 19 August 2013

* Correspondence: wolf.reik@babraham.ac.uk
[1]Epigenetics Programme, The Babraham Institute, Cambridge, CB22 3AT, UK
Full list of author information is available at the end of the article