

PRESS RELEASE

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For immediate release

Singapore scientists discover new regulators that maintain embryonic stem cells' unique epigenetic character

Cross talk between two molecular mechanisms maintains embryonic stem (ES) cells' unique characteristics of self-renewal and pluripotency, Singapore scientists reported in the Oct. 15th issue of *Genes & Development*.

This study is the first to determine that Jmjd1a and Jmjd2c genes enable ES cells to duplicate themselves endlessly and specialize into any cell type needed in the body. These regulators of ES cells were discovered by scientists at the Genome Institute of Singapore (GIS) and the National University of Singapore (NUS).

These findings built upon the scientists' previous research, published last month in the journal *Cell Stem Cell*, about the simultaneous presence of protein modifications that keep human ES cells primed and poised, ready to differentiate.

In the studies described in the *Genes & Development* paper, the researchers tested the Jmjd1a and Jmjd2c proteins' contribution to "stemness" by deleting each protein from laboratory cultures of mice ES cells. The ES cells proceeded to differentiate and ceased self-renewal.

The cross talk identified by the researchers include two participants, one of which is a network of proteins that transcribe genes' DNA recipes into the RNA language that cells need to manufacture proteins. The other participant, epigenetic enzymes, modify the activity patterns of genes in both ES cells and mature adult cells.

Epigenetic enzymes remove molecular obstacles to gene expression by attaching to and then modifying the tightly wound bundle of protein material called histones that package and compress the DNA in the nucleus of each human cell.

"This research is the first to show that epigenetic regulators play essential roles in embryonic stem cells and represents a new regulatory pathway that the embryonic stem cell uses to counteract the inappropriate silencing of key pluripotency genes." said Ng Huck Hui, Ph.D., senior group leader at GIS and a member of the Singapore team that conducted this research.

He and his colleagues also revealed that the Jmjd1a and Jmjd2c genes are bona fide targets of one of the four transcription factors that are known to be crucial to mouse ES cell pluripotency. Pluripotency disappeared when the transcription factor, named Oct4, was repressed in the ES cells. The results indicate that Oct4 may

safeguard the ES cells' ability to differentiate into any cell type by boosting the activity of epigenetic genes.

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Notes to Editor

Research publication:

The research findings described in this press release can be found in *Genes & Development* "**Jmjd1a and Jmjd2c histone H3 lysine 9 demethylases regulate self-renewal in embryonic stem cells**" published on 15 October 2007.

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About the Genome Institute of Singapore:

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The Genome Institute of Singapore (GIS) is a member of the Agency for Science, Technology and Research (A*STAR). Established in 2001, the research institute's mission is to be a world-class genomics institute and a centre for genomic discovery. GIS pursues the integration of technology, genetics and biology towards the goal of individualized medicine. The genomics infrastructure at GIS is utilized to train new scientific talent, to act as a bridge between academic and industrial research, and explore scientific questions of high impact.