Genome Institute of Singapore
A*STAR

MEDIA RELEASE

EMBARGOED UNTIL 31 JULY 2015 / 0000 (SST)

31 JULY 2015

SINGAPORE SCIENTISTS DISCOVER A MOLECULAR CELL CYCLE CLOCK THAT CONTROLS STEM CELL POTENCY

Findings on cell differentiation controls can advance understanding of stem cells

Singapore — Singapore scientists from A*STAR's Genome Institute of Singapore (GIS) have, for the first time, found further evidence of how the differentiation of pluripotent cells is tied to and controlled by the cell cycle clock. This deeper understanding of how cells become differentiated is extremely important when considering therapeutic potentials.

Embryonic stem cells (ESCs) are cells that have not differentiated into specific cell types, and are said to be in a pluripotent state. The cell cycle is divided into four phases: G1, S, G2 and M[1]. Previous studies have shown that cell differentiation of ESCs is initiated only in the G1 phase, attributed to G1-specific properties that contribute to lineage specification. The absence of these properties in the other three phases was believed to passively hinder differentiation.

This study, using high-throughput screening, provides the first evidence that during the S and G2 phases, the ESCs are more potent towards maintaining its stemness; that is, they actively resist differentiation.

Additionally, the scientists found that in instances of DNA damage, ESCs do not differentiate, so as to prevent the formation of specialised (differentiated) cells with compromised genomic integrity.

Findings from the study were published in the scientific journal *Cell*.

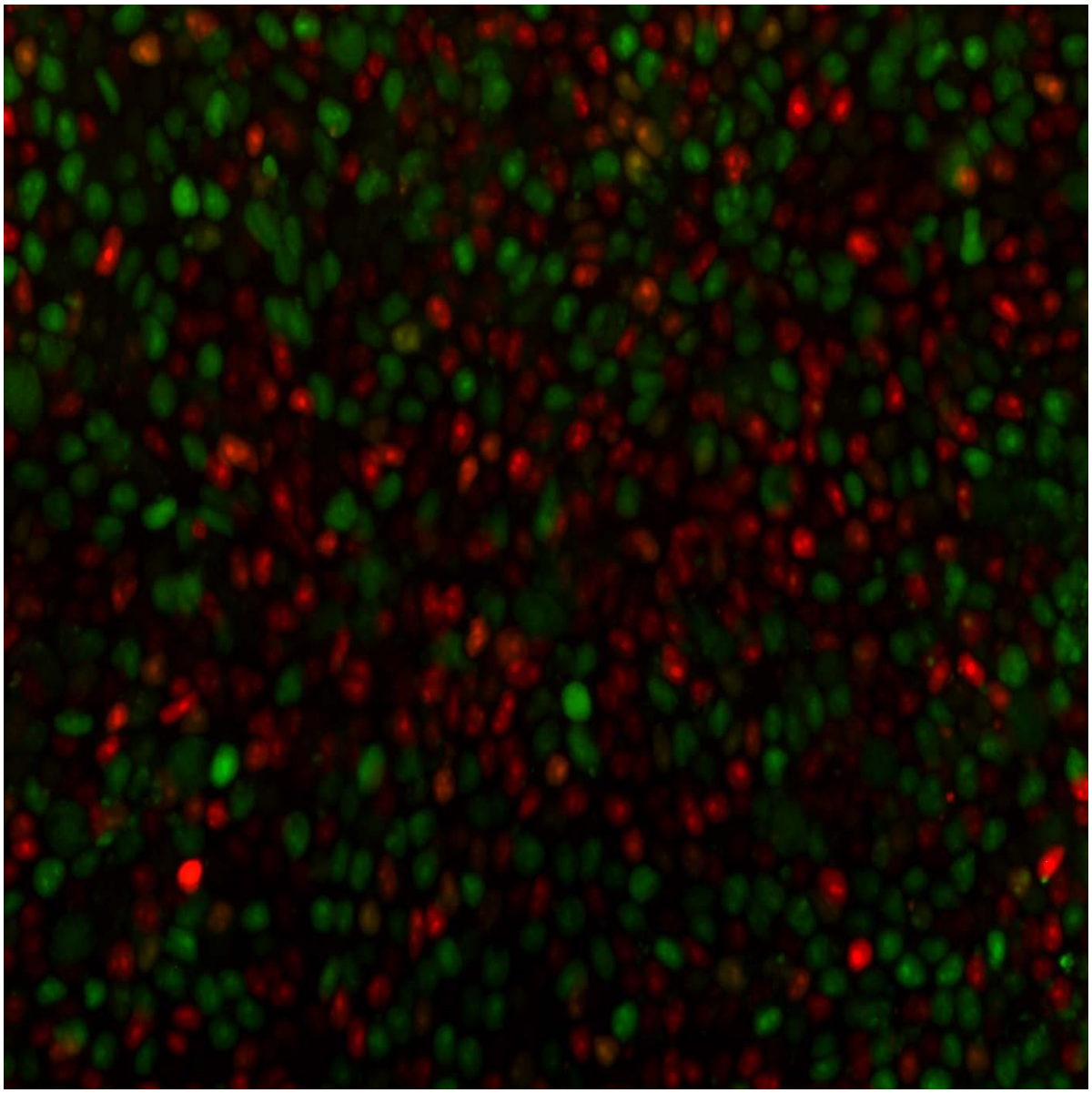
"Many studies have been devoted to looking at what keeps the ESCs in their undifferentiated state. Hence, to address a gap in the understanding of cell differentiation, our team at the GIS decided to focus on what regulates the ESCs' exit from their pluripotent state," said lead author of the research, Dr Kevin Gonzales, Post Doctoral Fellow at the Stem Cell and Regenerative Biology at GIS. "Moreover, most functional screens are carried out in mouse ESCs. The only functional screen on human ESCs was published in 2010 from our laboratory at the GIS. This latest study was also performed on human ESCs, making it more clinically relevant than studies using mouse ESCs."

[1] Cell cycle stages: (a) G1, first gap phase in preparation for DNA replication (G1); (b) S, DNA replication phase; (c) G2, second gap phase in preparation for cell division; (d) M, mitosis [cell division] phase.

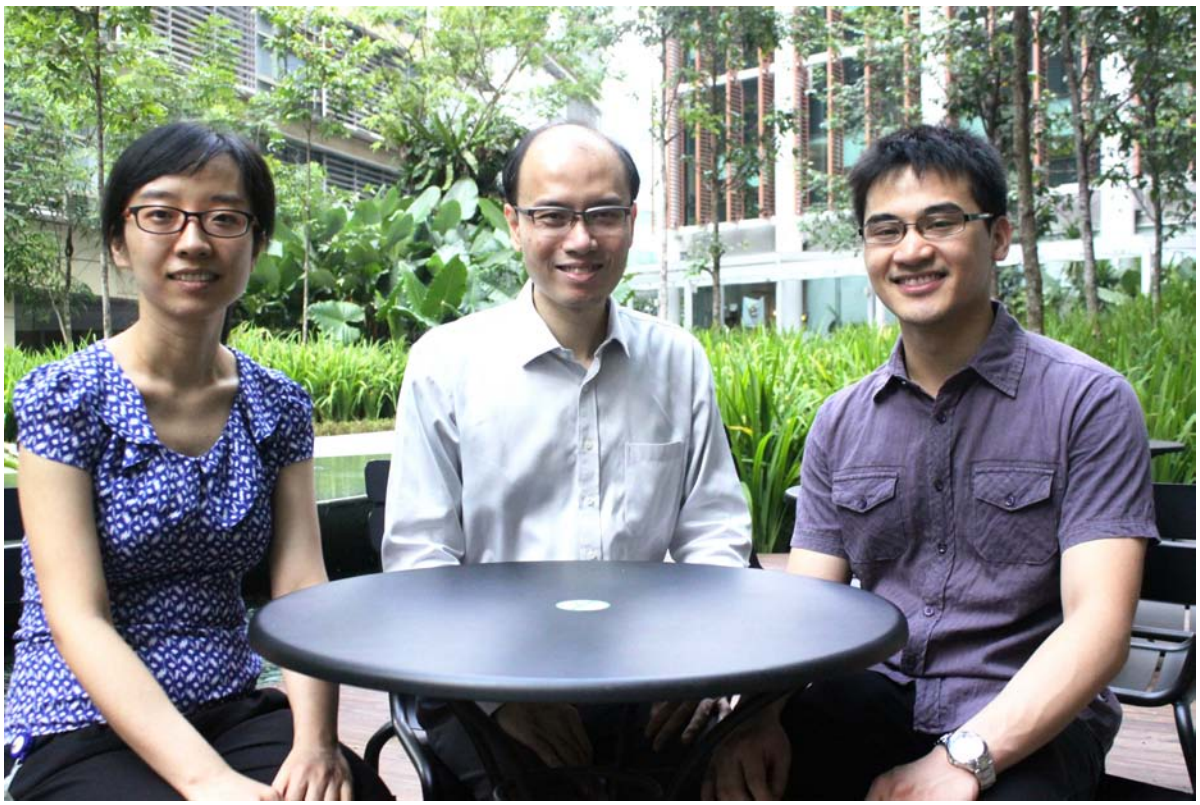
Co-lead author Research Fellow Dr Liang Hongqing at GIS' Stem Cell and Regenerative Biology added, "Our research has shifted the current paradigm from a G1-phase centric view in stem cell regulation to a balanced view that different cell cycle phases perform different roles to orchestrate the stem cell fate."

GIS Executive Director Prof Ng Huck Hui said, "Knowing that the S and G2 phases employ active pathways to prevent differentiation of ESCs, we can propose that, conversely, the absence of these pathways contributes to G1 phase amenability towards differentiation. This is truly an exciting and huge step forward in the study of cell pluripotency to advance fundamental understanding of human stem cells."

IMAGES



Human ESCs with fluorescence reporters aid the discovery of novel regulators of stem cell potency



(L to R) Dr Liang Hongqing, Prof Ng Huck Hui and Dr Kevin Gonzales

---

Notes to Editor:

The research findings described in the media release can be found in the scientific journal *Cell*, under the title, “Deterministic restriction on pluripotent state dissolution by cell cycle pathways" by Kevin Andrew Uy GONZALES[1,2,*], Hongqing LIANG[1,*], Yee-Siang LIM[1], Yun-Shen CHAN[1], Jia-Chi YEO[1,6], Cheng-Peow TAN[1], Bin GAO[1], Beilin LE[1,3], Zi-Ying TAN[1,5], Kok-Yao LOW[6], Yih-Cherng LIOU[2,5], Frederic BARD[3,4] and Huck-Hui NG[1,3,5,6,#]

1. Stem Cell and Regenerative Biology, Genome Institute of Singapore, 60 Biopolis St, Singapore 138672
2. NUS Graduate School for Integrative Sciences and Engineering, National University of Singapore, 28 Medical Drive, Singapore 117456
3. Dept of Biochemistry, National University of Singapore, 8 Medical Drive, Singapore 117597
4. Institute of Molecular and Cellular Biology, 61 Biopolis Drive, Singapore 138673
5. Dept of Biological Sciences, National University of Singapore, 14 Science Drive 4, Singapore 117597
6. School of Biological Sciences, Nanyang Technological University, 60 Nanyang Drive, Singapore 639798

* These authors contributed equally to this work.

\# Corresponding author: NG Huck Hui
Genome Institute of Singapore, 60 Biopolis St, Singapore 138672
Tel: +65 68088145, Email: nghh@gis.a-star.edu.sg

For media queries and clarifications, please contact:

Ms Winnie Lim
Head, Office of Corporate Communications
Genome Institute of Singapore, A*STAR
Tel: +65 6808 8013
Email: limcp2@gis.a-star.edu.sg

About the A*STAR's Genome Institute of Singapore (GIS)

The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit: www.gis.a-star.edu.sg

About the Agency for Science, Technology and Research (A*STAR)

The Agency for Science, Technology and Research (A*STAR) is Singapore's lead public sector agency that spearheads economic oriented research to advance scientific discovery and develop innovative technology. Through open innovation, we collaborate with our partners in both the public and private sectors to benefit society.

As a Science and Technology Organisation, A*STAR bridges the gap between academia and industry. Our research creates economic growth and jobs for Singapore, and enhances lives by contributing to societal benefits such as improving outcomes in healthcare, urban living, and sustainability.

We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and Research Institutes, the wider research community and industry. A*STAR oversees 18 biomedical sciences and physical sciences and engineering research entities primarily located in Biopolis and Fusionopolis.

For more information on A*STAR, please visit www.a-star.edu.sg