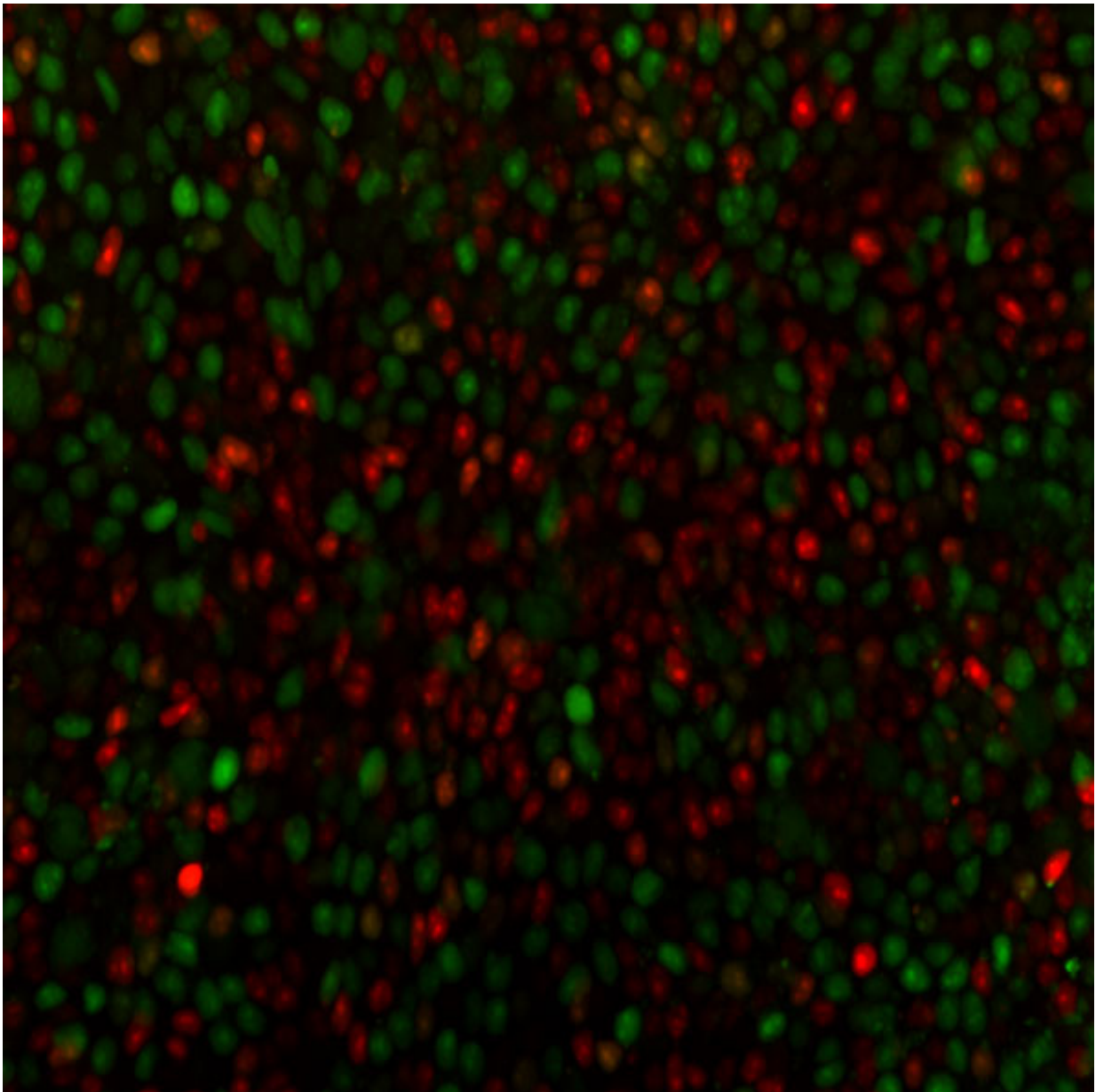


Scientists discover molecular cell cycle clock that controls stem cell potency

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Human ESCs with fluorescence reporters aid the discovery of novel regulators of stem cell potency. Credit: A*STAR

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. 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."

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](#)."

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