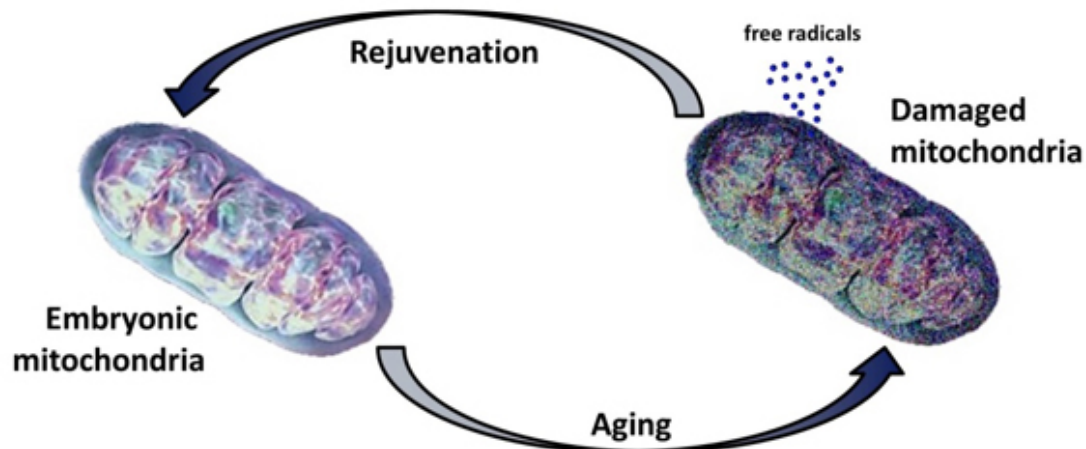


Singapore scientists discover rejuvenation factors

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Mitochondria during cellular aging. Credit: A*STAR

Scientists from A*STAR's Genome Institute of Singapore (GIS) have discovered metabolic rejuvenation factors in eggs. This critical finding furthers our understanding of how cellular metabolism changes during

aging, and during rejuvenation after egg fertilisation.

When a sperm fertilises an egg to create a baby, two [adult cells](#) combine to form a new embryo. A similar process of combining an egg's cytoplasm with an adult cell nucleus led to the cloning of Dolly the sheep. However, the metabolic factors underlying this fascinating process had remained unclear.

A new study from GIS suggests that old mitochondria – the oxygen-consuming metabolic engines in cells – are roadblocks to cellular rejuvenation. By tuning up a gene called Tc11, which is highly abundant in eggs, researchers were able to suppress old mitochondria to enhance a process known as somatic [reprogramming](#), which turn adult cells into embryonic-like stem cells.

GIS researchers found that Tc11 does its job by suppressing mitochondrial polynucleotide phosphorylase, thereby inhibiting mitochondrial growth and metabolism.

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

Stem cell researchers had known that egg (or oocyte) cytoplasm contains some special unknown factors that can reprogramme adult cells into embryonic-like stem cells, either during egg-sperm fertilisation or during artificial cloning procedures like those that created Dolly the sheep. While the Nobel Prize winner Dr Shinya Yamanaka had invented a technology called induced [pluripotent stem cell](#) (iPSC) reprogramming to replace the ethically controversial oocyte-based reprogramming technique, oocyte-based reprogramming was still deemed superior in complete cellular reprogramming efficiency.

To address this shortfall, the GIS team led by Dr Khaw Swea-Ling, Dr

Lim Bing and Dr Ng Shyh-Chang combined oocyte factors with the iPSC reprogramming system. Their bioinformatics-driven screening efforts led to two genes: Tc11 and its cousin Tc11b1. After a deeper investigation, the team found that the Tc11 genes were acting via the mitochondrial enzyme, Pn Pase.

"We were quite surprised, because nobody would have thought that the key to the oocyte's reprogramming powers would be a mitochondrial enzyme. The stem cell field's conventional wisdom suggests that it should have been some other signalling genes instead," said corresponding author of the research, Dr Ng Shyh-Chang.

Tc11 is a cytoplasmic protein that binds to the mitochondrial enzyme Pn Pase. By locking Pn Pase in the cytoplasm, Tc11 prevents Pn Pase from entering mitochondria, thereby suppressing its ability to promote mitochondrial growth and metabolism. Thus, an increase in Tc11 suppresses old [mitochondria](#)'s growth and metabolism in adult cells, to enhance the somatic reprogramming of adult cells into embryonic-like [stem cells](#).

Cracking the mystery of reprogramming factors in oocytes is an important milestone. These new insights could boost efficacy of the alternative, non-oocyte-based iPSC techniques for stem cell banking, organ and tissue regeneration, as well as further our understanding of how [cellular metabolism](#) rejuvenates after egg-sperm fertilisation. This could help address both the aging and the fertility problems of modern societies.

GIS Executive Director Prof Ng Huck Hui said, "This is an exciting step forward in the study of cellular aging. Although accumulated defects in mitochondrial metabolism were known to cause cellular aging, no solutions were available. Shyh-Chang's team has uncovered a molecular pathway to solve this problem."

More information: *Cell Reports*: [www.cell.com/cell-reports/full...
2211-1247\(15\)00792-5](http://www.cell.com/cell-reports/full...2211-1247(15)00792-5)

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