

NUS team discovers way to rejuvenate eggs of older women

Researchers' breakthrough could boost success of assisted reproductive tech

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A woman's eggs age a lot faster than the rest of her, cutting her chances of giving birth to a baby as she gets older.

But researchers from Singapore have made a breakthrough in reversing the age of women's eggs, paving the way for greater success in assisted reproductive technologies such as in-vitro fertilisation (IVF).

While still restricted to the petri dish for now, the research findings offer renewed hope for older women looking to take motherhood off the back burner after taking time to focus on other life priorities, including their careers.

The discovery centres on how the follicular environment plays a crucial role in the development and quality of a woman's oocytes, or immature egg cells.

Putting a young egg cell in an aged follicle aged it, while the reverse actually rejuvenated older egg

cells, scientists from the Mechanobiology Institute (MBI) at the National University of Singapore and the NUS Bia-Echo Asia Centre for Reproductive Longevity and Equality (ACRLE) found.

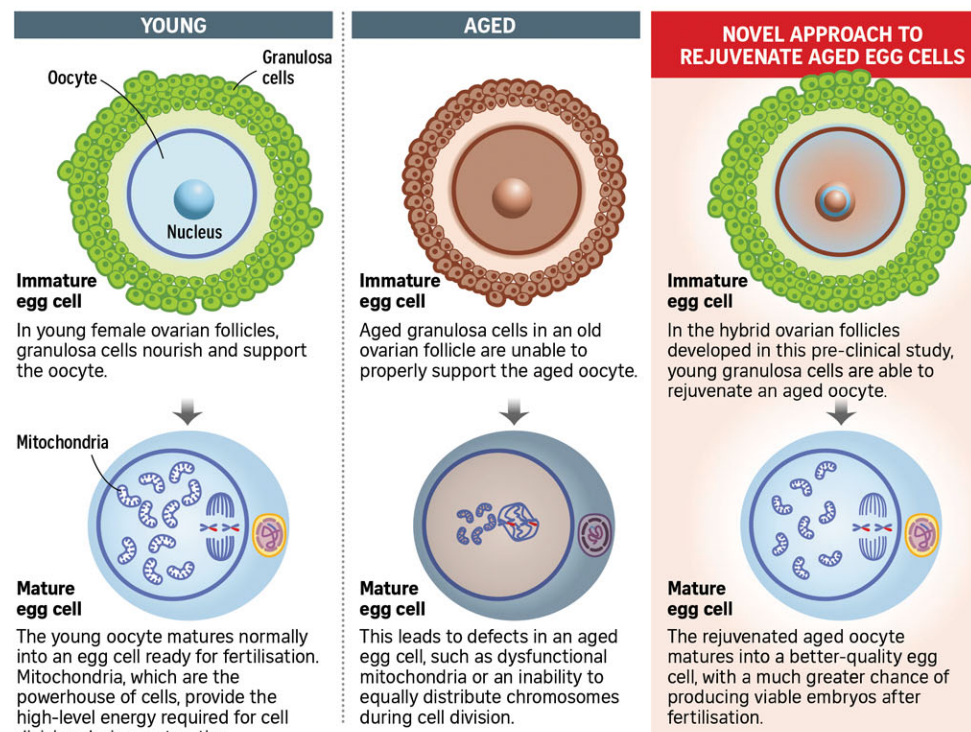
Mechanobiology is an emerging multidisciplinary field that studies how cells and tissues sense and respond to mechanical signals or forces that regulate a wide range of biological activities, such as cell migration, cell proliferation and single molecule behaviour.

A follicle is a small, fluid-filled sac in the ovaries that contains an oocyte. Several follicles begin to develop during each menstrual cycle, but usually just one egg cell fully matures and is released during ovulation.

"We have been intrigued by the process of ageing in the human cells, in particular the ageing of oocytes because they grow older much faster than any of the other human cells," MBI director Rong Li told *The Straits Times*. "We want to know if it is possible to slow down or reverse this ageing process."

Reversing the age of a human egg

Female reproductive ageing is a natural process that leads to a decline in egg quantity and quality. With more women delaying childbirth, reversing the ageing of oocytes, or immature egg cells, has become important for successful pregnancy and birth.



Source: NATIONAL UNIVERSITY OF SINGAPORE STRAITS TIMES GRAPHICS

Oocyte quality declines with age, beginning at around age 32 and more rapidly after 37, resulting in a lower rate of successful fertilisation and a higher chance of miscarriage or genetic disorders in the resulting embryos.

The team found that the young oocyte, when introduced to an aged follicle – similar to those in older women – became aged and lost its quality and developmental potential very quickly as "the aged follicular environment was not transferring the energy or nutrients it need-

ed", said Dr Wang Haiyang, a senior research fellow at MBI.

"The young oocyte soon took on the characteristics of an aged oocyte and showed increased signs of ageing, such as a rise in indicators of DNA damage and other factors linked to cell death. This was where I started wondering if the reverse could happen," Dr Wang said.

The team then studied how an aged oocyte developed in a young follicular environment.

"We found that the young granulosa cells helped to restore the aged

oocyte," Professor Li said, referring to the cells that make up ovarian follicles, supplying an oocyte with essential nutrients as it grows and matures.

"There was improvement in the function and health of oocyte mitochondria (the powerhouse of the cell), energy and cellular metabolism," she added.

However, the study found that oocyte ageing was significantly – but not completely – reversed, and the team aims to investigate why that is so, next, Prof Li said.

The novel approach and findings on the impact of the follicular environment on oocytes were published in peer-reviewed journal *Nature Aging* on Sept 9.

The next stage involves turning this finding into a technology to enhance the success of assisted reproductive technologies, including IVF, Prof Li said.

"The findings from this study provide a proof-of-concept and the basis for the development of non-invasive cell-based strategies to improve the quality of eggs from older women or women whose reproductive ability is affected by other health conditions.

"An analogy of this is sending the (aged) oocyte to a rejuvenating spa and once the oocyte is partially renewed, fertilise it in the lab and then implanting the embryo back into the womb through IVF. This way, I believe the number of successes will be high," she added.

More couples have been seeking assisted reproductive technology here, with some experts saying the trend of couples marrying at a later age is one reason more women need help conceiving, since fertility declines with age.

Women were marrying for the first time at a median age of 29.3 years in 2022, up from 28 in 2012.

The median age of first-time mothers has also risen over the years, from 30.8 years in 2019 to 31.6 years in 2023.

In terms of much older mothers, there were 19 women aged at least 50 who gave birth here in 2023 – three of whom were at least 55 years old.

Dr Huang Zhongwei, deputy director of ACRLE, said of the findings: "This advancement is crucial, as it empowers women to maintain optimal reproductive health regardless of whether they choose to conceive later in life.

"The implications of this research and the work we do at ACRLE could redefine fertility preservation strategies, providing women with greater control over their reproductive timelines while ensuring healthier outcomes for future generations."

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More women aged 50 and older having babies

The boundary of motherhood has shifted over the past few years as more women aged 50 and above are having babies.

In 2023, 19 women aged 50 or older gave birth, three of whom were at least 55 years old then, according to the Immigration and Checkpoints Authority's annual report.

Between 1989 and 2009, six women aged 50 or older had babies. This number increased more than five times between 2010 and 2019, with 33 such women giving birth.

Among the 33 women was a 58-year-old who had twins in 2016. She is believed to be Singapore's oldest woman to give birth.

The most well-known woman in Singapore to have a baby at the age of 50 or older is veteran actress and

getai singer Liu Lingling.

She underwent in-vitro fertilisation treatment and gave birth to her son Caleb in 2013 at the age of 50.

Other celebrities who had babies after turning 50 include singer Janet Jackson, who was 50 when she had her son Eissa in January 2017; model Naomi Campbell, who was 53 when she had her son in June 2023; and actress Cameron Diaz, who was 51 when she welcomed her second child, a boy named Cardinal, in March 2024.

Liu revealed in a television interview in 2022 that she had high blood pressure, high cholesterol and high blood sugar during pregnancy – all of which made it dangerous for her to give birth.

Obstetrician and gynaecologist

Christopher Chong said that what Liu experienced is typical of the risks for an older woman carrying a pregnancy.

"As a woman ages, the number and quality of her eggs decline, making it increasingly difficult for her to conceive a child. Once a woman hits 50, her chances of conceiving naturally are around 1 per cent. This means only one in 100 women at that age and older will succeed in having a baby without fertility treatments," he said.

"For these older mothers, there would be increased risks of miscarriage, premature birth, foetal abnormalities and intra-uterine growth restriction (when a baby in the womb does not grow at the expected rate)."

During the birth, said Dr Chong, there would also be increased risks of caesarean section delivery; amniotic fluid embolism, which is a severe allergic reaction to amniotic fluid getting into the bloodstream; and mother and child trauma.

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Veteran actress and getai singer Liu Lingling with her son Caleb in 2022. She underwent in-vitro fertilisation treatment and gave birth to him in 2013 at the age of 50.
ST PHOTO: KUA CHEE SIONG