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Chromosome key to later fertility

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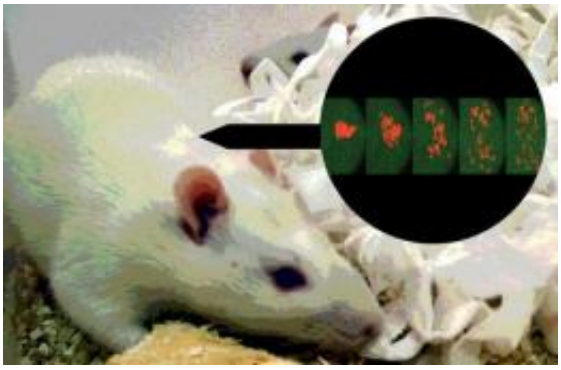

Chromosome segregation process in genetically modified mice. Segregation was brought about by the introduction of the enzyme to mice egg cells, triggering the opening of the protein ring holding the chromosomes.

(PhysOrg.com) -- New research at Oxford University has shed light on how mammalian egg cells divide. The findings may lead to improvements in women's chances of giving birth to healthy babies as they get older.

After the age of 33, the likelihood of a woman producing healthy eggs and embryos declines dramatically but little is known of the reasons why.

In younger women, the pairing off, or segregation, of chromosomes in precursor cells usually produces eggs with a complete set of chromosomes. Fertilisation of these eggs would tend to produce viable embryos.

But, as women age, chromosome segregation becomes faulty and eggs can be produced with the wrong number of chromosomes.

This increases the probability of miscarriage or birth defects such as those associated with Down's syndrome. But if ways can be found to safeguard chromosome division for longer, this deterioration could be delayed.

‘If we find it’s possible for egg precursor cells to regenerate the proteins and the structures responsible for chromosome cohesion we could, in the long-term, develop therapeutic advances giving older women a better chance of giving birth to healthy children,’ Dr Kikuë Tachibana-Konwalski of Oxford’s Department of Biochemistry says.

‘By the time women reach their 40s, a third of their eggs may already have the wrong number of chromosomes. So as society changes and more women concentrate on their careers and delay childbirth, our research could be extremely important.’

Dr Tachibana-Konwalski’s study has revealed which proteins are responsible for binding chromosomes in mammalian egg cells. Her research group, funded by the Medical Research Council, Cancer Research UK and the Wellcome Trust, also found that it is possible to trigger the separation of chromosomes by destroying these proteins.

In a paper published in the journal *Genes & Development*, Dr Tachibana-Konwalski and colleagues describe how the introduction of an enzyme into the egg cells of genetically modified mice can trigger the opening of the protein ring holding together chromosomes and in turn trigger chromosome segregation.

Together with Professor Kim Nasmyth, Head of Oxford’s Department of Biochemistry, and Dr David Adams of the Wellcome Trust Sanger

Institute, Dr Tachibana-Konwalski suspects that the deterioration of this protein ring, which contains the protein Rec8, is causing chromosome mis-segregation in the eggs of older women.

Finding a way of regenerating the chromosome cohesion brought about by Rec8 and enabling the proteins to bind for longer, could increase the chances of older women producing healthy embryos.

It is unlikely that chromosome cohesion is regenerated over a few weeks, the research shows, but future studies will assess whether it might take place over a longer period.

'The most mysterious cells in the body are the egg cells in women,' says Dr Tachibana-Konwalski. 'They provide nearly everything for the next generation but are difficult to study because there are so few of them. If we find that chromosome cohesion can be regenerated it will be a hugely significant discovery, especially for women who want to have children in their late thirties and forties.'

More information: Paper online: genesdev.cshlp.org/content/24/22/2505

Provided by Oxford University