Lockdown genes to reduce IVF failure rates

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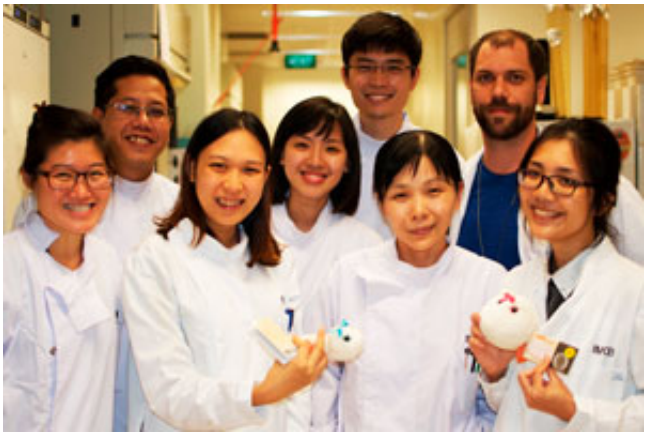

A*STAR scientists in the Developmental Epigenetics and Disease group. Credit: A*STAR Institute of Molecular and Cell Biology

Embryos kickstart a vibrant genetic program to thrive, but if the wrong genes are active the cells can self-destruct. A*STAR scientists have discovered one of the genes that needs to be tightly locked down for an embryo to develop: a finding that could improve IVF success rates.

Human egg and sperm cells have their genes trained on a single purpose – to fertilize. Once their mission is complete, the developing embryo begins the complicated genetic program that turns a single cell into a healthy fetus.

This program is possible thanks in part to epigenetic changes to the DNA, such as the removal of methyl group 'locks' by enzymes, which

allows many more genes to be read.

Some specialized genes however need to be locked down during development, as their genetic messages cause problems for the embryo.

"Everything that goes wrong in embryos has the potential to cause infertility or early pregnancy abortions," explains Daniel Messerschmidt from the A*STAR Institute of Molecular and Cell Biology. "We are keen to discover the genomic locations which impact on that development."

Messerschmidt's team previously discovered that a protein called Trim28 locks methyl groups to certain regions in the genome. Now, the researchers looked for the targets of Trim28 to find what genes lies within these regions.

The scientists sequenced the RNA of more than 30 embryos lacking Trim28 and discovered that a gene called Rbmy1a1 was unusually active.

"It's an interesting gene which is not expressed anywhere in the body during development except for spermatogonia in the testes – it has no place to be expressed in the embryo," says Messerschmidt. He proposes that the enzyme encoded by Rbmy1a1 produces mRNA transcripts which are harmful to the developing embryo.

Messerschmidt's team is now looking for more of these 'special attention' genes. If the activity of detrimental genes such as Rbmy1a1 can be detected before an embryo is implanted, then it could improve rates of IVF success, says Messerschmidt.

"We want to find out whether we can do epigenetic diagnostics in the same way as when we screen for a suspected genetic disease," he says. "Ultimately, having an overall understanding of these processes will give

us a basis for what to look at."

Messerschmidt adds that an epigenetic diagnostic tool for embryos may allow doctors to compare IVF methods which differ between labs. "If we can compare different methods, perhaps we can point doctors to techniques that improve efficiency," he says.

More information: Abhishek Sampath Kumar et al. Loss of maternalTrim28causes male-predominant early embryonic lethality, *Genes & Development* (2017). DOI: 10.1101/gad.291195.116

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