MedicalXpress

Gene involved in sperm-to-egg binding is key to fertility in mammals

May 1 2012

Experts from Durham University have identified a new gene that could help the development of fertility treatments in humans in the future.

Scientists from Durham University, UK, and Osaka University, Japan, looking at fertility in mice, have discovered for the first time that the gene, which makes a protein called PDILT, enables sperm to bind to an egg, a process essential to fertilisation.

The team found that when the gene was 'switched off' in male mice, less than three per cent of females' eggs were fertilised compared to more than 80 per cent in mice when the gene was left switched on.

It is the first time that a gene of this type has been linked to fertility.

The researchers also found that the cumulus cells, a cluster of cells surrounding and protecting an egg, play an important role in fertility - their presence enables sperm to bind properly to an egg.

Although the research and findings are at an early stage, the researchers now hope to look at how the gene affects sperm-to-egg binding in humans. The findings are published in the journal PNAS, *Proceedings of the National Academy of Sciences*.

The discoveries could pave the way for the development of new fertility treatments for humans that could help to reduce the cost and improve the effectiveness of in vitro fertilisation (IVF). They could also assist

research into new contraceptive techniques that deactivate the gene and prevent sperm reaching an egg and binding to it.

Dr Adam Benham, School of Biological and Biomedical Sciences, Durham University, said: "The protein is an essential part of the navigation system of sperm. It helps sperm swim through the oviduct to the egg and without it sperm get stuck. Our results show that navigating the oviduct is an important part of the fertilisation process.

"Like any navigation system, you have to programme where it is that you want to go and this protein plays an essential role in getting sperm to the right destination, in good shape, and in good time."

The researchers found the gene a few years ago through a database search for new genes of the PDI family. Following extensive research, they established that the gene made an important protein in the testes.

The PDILT gene, part of the PDI family, helps another gene product called ADAM3 to form and assemble correctly, and then to reach the surface of a sperm, thereby equipping it with the right tools and machinery to navigate and make contact with an egg.

The new findings show the importance of PDILT in the process of sperm-to-egg binding and in enabling sperm to swim past the uterus, ascend the oviduct and to get through the sticky outer layers of an egg.

The team honed in on the role of the protein by switching it off in mice and tracking the ability of sperm to bind to and fertilise eggs in Petri dishes and in mice. They noticed that sperm from mice with the gene switched off will not bind to a bare egg, but will bind to an egg surrounded by cumulous cells.

Dr Benham said: "We now hope to discover how the PDILT protein

affects fertility in humans. Mutations in the gene may be responsible for unexplained male fertility problems and further research may aid more effective IVF treatment."

Dr Masahito Ikawa from Osaka University, Japan, added: "This protein is essential for sperm to migrate successfully and is required for fertility. The next step is to see how this protein works with other proteins to control the sperm binding and fusion process."

More information: *PNAS* March 6, 2012 vol. 109 doi: 10.1073/pnas.1117963109

Provided by Durham University