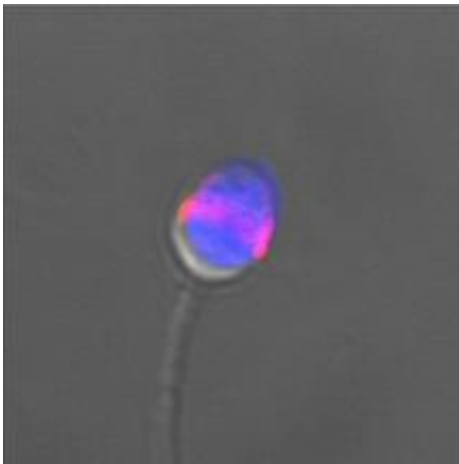


Mutation causing one type of male infertility found

July 21 2009



The PLC zeta protein is located in a band around the sperm cell, shown in red.

(PhysOrg.com) -- A genetic mutation that lies behind one type of male infertility has been discovered by researchers at Oxford University, Ghent University in Belgium, and the University of Massachusetts, Amherst in the USA.

The discovery, published in the journal *Human Reproduction*, may provide a new approach to help some couples that have been unsuccessful in IVF treatments, and could potentially lead to the development of a male contraceptive pill.

The mutation was found in a man known to have a defect in his [sperm](#)

following initially unsuccessful IVF treatment at a clinic at Ghent University Hospital.

The mutation lies in one specific [protein](#) present in sperm called PLC zeta. Recent research, in which the Oxford team played a significant role, has shown that sperm transfers PLC zeta to the egg on fertilisation. The protein initiates a process called ‘egg activation’ which sets off all the biological processes necessary for development of the embryo.

‘An [egg cell](#) before fertilisation is in a state of suspended animation. All the biological processes that occur in the growth and development of an embryo are on pause,’ explains Dr John Parrington of the Department of Pharmacology at the University of Oxford. ‘At the moment of fertilisation, when a sperm fuses with the egg, the egg bursts into life. It’s like a Prince waking Sleeping Beauty.’

The research team, funded by the Medical Research Council and Belgian funding agencies, looked at sperm samples from nine men at the same clinic where an IVF procedure known as intracytoplasmic sperm injection, or ICSI, had been unsuccessful. In each of these cases, the eggs had failed to activate.

ICSI involves the direct injection of the sperm into the egg, and is often used in IVF treatment to help ensure fertilisation. However, in two to three per cent of cases where ICSI is used, egg activation doesn’t occur and the fertilised egg doesn’t develop. ICSI was used in 47% of all IVF treatments in the UK in 2006, or over 20,800 cases. So potentially around 600 couples a year in this country could find that they can’t have children in this way.

The scientists conducted a series of experiments to test how well the protein PLC zeta in these samples was functioning. They found that one man had a mutation in the gene for PLC zeta. The mutation was at a

critical point and produced a mutant form of the protein that could no longer trigger egg activation. This is the first genetic mutation discovered to explain this type of male infertility.

Other samples showed other problems in PLC zeta: there was not enough protein, it was located in the wrong part of the sperm cell, or a truncated version was produced.

'We have found that some men are infertile because their sperm fail to activate eggs,' says Dr Kevin Coward of the Nuffield Department of Obstetrics and Gynaecology at Oxford University, who was also involved in the research. 'Even though the sperm fuses with the egg, nothing happens. The sperm lack a proper functioning version of the PLC zeta protein involved.'

The Oxford and Ghent University researchers have also demonstrated that it should be possible to overcome this problem. For those couples that need it, providing a working version of the PLC zeta protein in IVF/ICSI treatment should offer them the chance to conceive.

The researchers found that mouse egg cells injected with a correct version of the gene for PLC zeta produce the protein for themselves, rather than relying on the sperm cell, and are successfully activated.

'This was a lab experiment and our method could not be used in a fertility clinic in exactly the same way,' cautions Dr Parrington. 'But in the future, if we could produce the PLC protein artificially, we could stimulate egg activation in a completely natural way. For those couples going through IVF treatment where ICSI has failed, it could give them the chance of a baby.'

Since PLC zeta has been shown to be crucial for a fertilised egg to develop into an embryo, a drug that inhibits the protein would be a good

candidate for a male contraceptive.

'It's a bit of a cliché in the field that every advance like this gets talked up as a possible new contraceptive pill for men,' says Dr Parrington. 'However, now we know that this one protein is absolutely critical at the point where life begins, we can think about finding drugs that stop this protein acting, while leaving all the other PLC proteins in the body unaffected. While this discovery is just an initial step and there is no guarantee of success, a targeted male pill that would not have any of the side effects of the female pill is a tantalising prospect.'

Provided by Oxford University ([news](#) : [web](#))

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