

# Infertility mechanism in males identified

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Large doses of a sperm protein that is ineffective in infertile males can be injected directly into eggs to kick-start fertilization, giving couples hope of conceiving.

A sperm [protein](#), called phospholipase C zeta (PLC $\zeta$ ), has been found to

be necessary for egg fertilization. The protein is ineffective in some [infertile men](#), according to new research by collaborators from Qatar University and Cardiff University in the UK.

The team was able to initiate the [fertilization process](#) in the lab by injecting [eggs](#) with a higher amount of the PLC $\zeta$  protein than naturally found in the sperm of infertile men. The results suggest that this type of infertility could become reversible.

"This study discovered that PLC $\zeta$  protein generated in the lab can successfully replace sperm and trigger the development of an egg up to the blastocyst embryo stage," says Michail Nomikos of Qatar University's College of Medicine. "We are currently developing a therapeutic agent to treat such cases of male infertility."

Sperm PLC $\zeta$  is an essential trigger of the first 'egg activation' stage of fertilization. The egg is in a dormant state until a sperm fuses with it, delivering the PLC $\zeta$  protein and stimulating the critical egg activation events that lead to early embryo development. This PLC $\zeta$  'spark of life' protein was discovered in 2002 by Tony Lai and his team at Cardiff University.



Michail Nomikos of Qatar University and colleagues are developing a diagnostic test for men with dysfunctional PLC $\zeta$  proteins, as well as potential tools to overcome this type of infertility in the lab. Credit: Qatar University

Recent clinical studies have reported that the sperm of some males fail to initiate fertilization despite having normal morphology and motility. Even though the sperm can fuse with an egg, nothing follows. Nomikos, Lai and their collaborators discovered that [sperm](#) from these men lack a properly functioning version of PLC $\zeta$ .

The team investigated the effects of a mutation in the gene that codes for PLC $\zeta$  on infertility. They found that injecting the mutated PLC $\zeta$

protein into mouse eggs, at levels comparable with those of infertile men, failed to spark the fertilization process. However, if they increased the amount of abnormal protein to higher levels than naturally present, the normal fertilization process began. The researchers suspect that the very high amount of protein somehow compensates for its impaired functioning.

"We hope that this work will lead to a PLC $\zeta$  therapy to help couples suffering from infertility to have the chance of a family," says Lai.

The group also plans to see if they can develop a tool to diagnose men with absent or dysfunctional PLC $\zeta$  protein.

Provided by Qatar University

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