Press release

Centre for Cellular and Molecular Biology

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Novel genes for male fertility

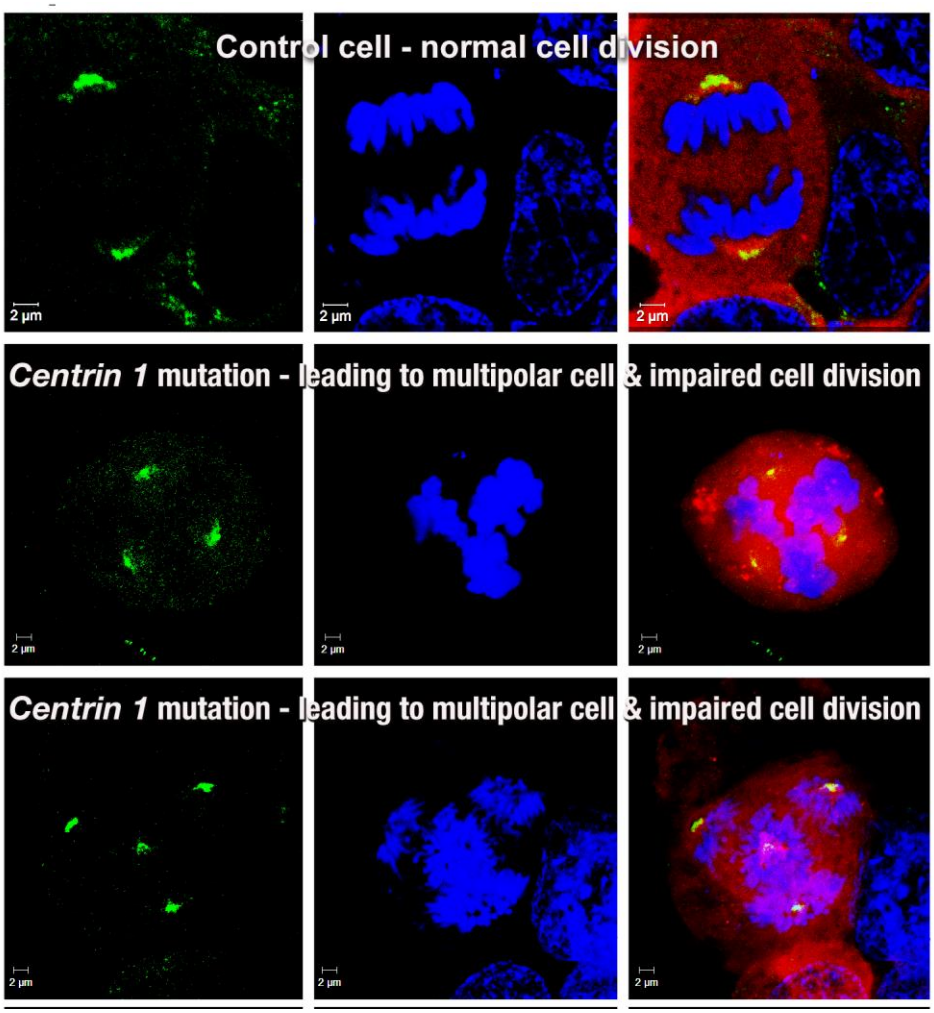
Approximately, one out of every seven couples are infertile worldwide. And, male infertility accounts for ~50% of these cases. The cases range from defects in the male reproductive system, deficiencies in semen quality, and hormonal imbalance. Injuries, infections, chronic illness, lifestyle choices and genetic factors can all lead to infertility in males. We, however, do not yet understand the details of how these parameters control fertility.

Dr. K Thangaraj's group at the CSIR-Centre for Cellular and Molecular Biology (CCMB), Hyderabad has been researching to understand the genetic causes of male infertility for the last two decades. They have shown earlier that about 38% males with infertility have specific regions missing or abnormalities in their Y chromosomes or mutations in their mitochondrial and autosomal genes.. Their new multi-institutional study focuses on the cause of infertility in the rest of the cases, which constitutes the majority of infertility-affected men. They have identified 8 novel genes that were defective in these men in India. The study has been recently published online in the journal *Human Molecular Genetics*.

Dr Sudhakar Digumarthi, lead author of the study, who was a PhD student of CCMB and presently scientist at ICMR-National Institute for Research in Reproductive and Child Health in Mumbai, said, "We first sequenced all the essential regions of all genes (around 30,000 of them) using next generation sequencing in 47 well-characterized infertile men. We then validated the identified genetic changes in about 1500 infertile men from different parts of India."

Dr Thangaraj, lead investigator of this study and presently Director of the DBT-Centre for DNA Fingerprinting and Diagnostics, Hyderabad said, "We identified a total of eight genes (*BRDT*, *CETN1, CATSPERD, GMCL1, SPATA6, TSSK4*, *TSKS* and *ZNF318*), that were not known earlier for their role in human male fertility". He further added that they have identified variations (mutations) in these genes that cause impaired sperm production leading to male infertility.

The researchers have characterized a mutation in one of the eight genes, Centrin 1 (*CETN1*), to understand how the mutation affects sperm production. They demonstrated the impact of *CETN1* mutation in cellular models and found that the mutation arrests cell division, causing insufficient sperm production.



“This study should be a reminder to the society that half of the infertility cases are due to problems in men. And many of them are due to genes that come from the parents, often mothers, of these men. It is wrong to assume a couple cannot bear children because of only the woman’s fertility,” remarked Dr Thangaraj.

Dr Vinay Kumar Nandicoori, Director, CCMB said, “The genetic causes established in this study could be used as potential diagnostic markers for male infertility, and development of improved management strategies for male infertility”.

Other institutions involved in this study are:

Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bengaluru; Institute of Human Genetics, University Hospital Düsseldorf, Heinrich-Heine-Universität, Germany; All India Institute of Medical Sciences, New Delhi; CSIR-Central Drug Research Institute, Lucknow; Institute of Reproductive Medicine, Kolkata; Indian Institute of Science Education and Research (IISER) Berhampur; Mamata Fertility Hospital, Secunderabad; DBT-Centre for DNA Fingerprinting and Diagnostics, Hyderabad.

The paper can be found online here:

https://academic.oup.com/hmg/advance-article/doi/10.1093/hmg/ddac216/6682817?guestAccessKey=420cea3d-32f4-4b72-b1c1-59ab558b8f2a

Or scan the below link to find the paper online:

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