

THE WALTER AND ELZA HALL INSTITUTE OF MEDICAL RESEARCH
and
THE MONASH INSTITUTE OF MEDICAL RESEARCH
Melbourne, Australia

MEDIA RELEASE - FOR IMMEDIATE USE

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Possible genetic cause of male infertility discovered

An international collaboration involving the Walter and Eliza Hall Institute (WEHI) and Monash Institute of Medical Research (MIMR) has shed valuable light on a possible genetic cause of male infertility.

The scientific team led by WEHI Scientist, Dr Hamish Scott found that mice with certain changes in their DNA and the proteins surrounding this genetic code did not produce sperm.

Important chemical modifications occur at conception when two sets of DNA meet from the egg and sperm. When the gene that regulates these modifications is disrupted in some way, the manner in which the DNA is packed into chromosomes is altered.

“The packaging of DNA is especially important for the production of eggs and sperm,” explained Dr Scott. “Consequently when this process is disturbed it can lead to problems of sterility and this is what we have observed in our male mouse model.”

“We also believe these genetic changes could explain the increased level of genetic disorders in children born from assisted reproductive technologies, as well as some disorders observed in cloned animals,” he said.

One in 25 Australian men suffers from poor fertility and one in 35 has no sperm at all. While

in many men this is due to overheating, physical damage to the testes, infections or drugs, in 40% of infertile men the cause of their disordered sperm production remains unknown.

“We have suspected that much of unexplained male infertility is due to genetic mutations in sperm producing genes,” said Dr Moira O’Bryan, Senior Scientist at MIMR. “Identifying the genes responsible has been the challenge and thus this discovery is a valuable one.”

“Understanding the cause of their infertility is psychologically important for some men, and this insight could also assist couples to make informed decisions when choosing assisted reproductive technologies [ART],” said Dr O’Bryan.

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While acknowledging that further studies are needed to translate this discovery in the mouse into humans, Dr O'Bryan is very optimistic about the possibility that this insight could minimize the risk of health problems in children born from ART.

“Men diagnosed as having this problem may select to use donor sperm, rather than risk passing the genetic disorder onto their offspring. Alternatively, in the future it may be possible to screen embryos in the laboratory for these genetic defects. Only embryos without this abnormality in their DNA would be implanted. This discovery provides valuable insight into minimizing the possibility of health problems in children born from ART.”

PhD student Kylie Webster from WEHI, who played an important part in this discovery team, said it was an exciting project to be involved in. “Tracing the far-reaching domino effects of upsetting the genes that regulate the packaging of DNA has been fascinating. However, further research is required.”

Other collaborators on the research paper which is to be published in the 15 April 2005 (hard copy) issue of the prestigious US-based journal *Proceedings of the National Academy of Sciences* included: Prince Henry's Institute of Medical Research, Melbourne; the Murdoch Children's Research Institute at the Royal Children's Hospital, Melbourne; the University of Queensland; Tampere University Hospital, Finland; the University Hospitals of Geneva, Switzerland; and the University of Tartu, Estonia.

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Following now: Media Backgrounder including graphic: The Value of DNA Packaging

MEDIA BACKGROUNDER:

The Value of DNA Packaging

In the cells of humans and animals, DNA is wrapped around specialized proteins. The DNA and proteins are chemically modified to tightly and correctly package the DNA into a cell nucleus.

Every individual has a unique DNA sequence – with its naturally occurring chemical modifications – that stores, replicates and transmits the genetic information that comprises every distinct individual.

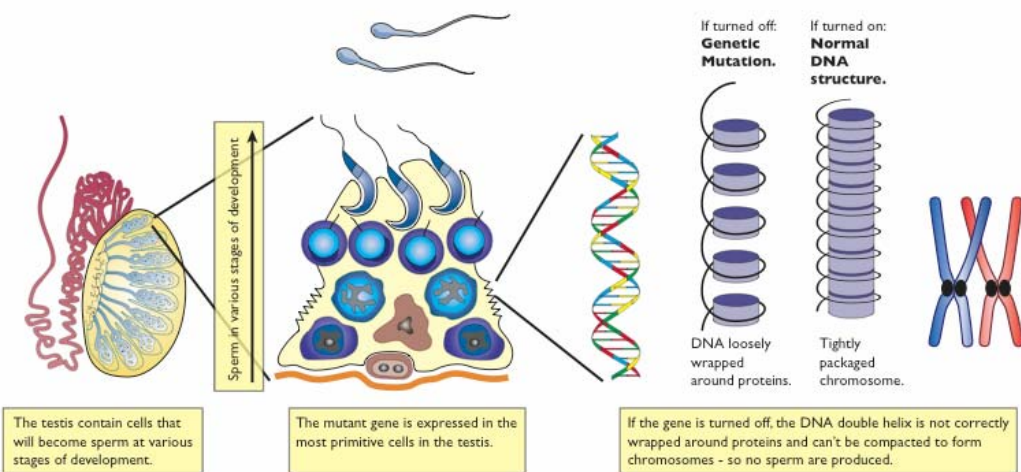
During the production of eggs or sperm, the chemical modifications are completely erased and then partially reset. Fertilization of the egg then creates a unique individual from the combination of genetic programs, newly introduced genetic data and environmental influences.

It has been established previously that such chemical disruptions can cause human genetic conditions such as obesity and cancer predisposition, while causing abnormalities in cloned animals.

Disruption of a gene involved in regulating chemical modifications has a range of effects. It upsets the modifications and alters how DNA and proteins are packed into chromosomes. As this packaging impacts on the production of eggs and sperm, naturally occurring defects in these genes can lead to male sterility. There is also a chance of genetic disorders in children born using assisted reproductive technologies.

In addition, the human genome is constantly under attack by viruses that often manage to have themselves integrated into the host's DNA and genome. Once infiltrated, the viruses attempt to replicate and spread within the genome. In fact, 45% of the human genome displays evidence of being derived from these attacks. Our body's method of defense against these attacks is to chemically modify and neutralize the virus genomes once they are inside our DNA. It is important because such viruses in the genome could be passed on to children with the heightened risk of genetic mutations and disease.

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