# Scientists develop the first model for investigating the origins of testicular cancer in humans

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Scientists have developed a model that will enable them to investigate, for the first time, how human testes develop in baby boys while they are in the womb. Until now it has been impossible to study testicular development during pregnancy in humans and this discovery will enable researchers to understand the processes that can lead to the onset of testicular germ cell cancer (TGCC) in young adult life, and how factors, such as common environmental chemicals, might play a role.

The research was carried out by Dr Rod Mitchell, clinical research fellow at the UK's Medical Research Council's Human Reproductive Sciences Unit at the University of Edinburgh, and is published online in Europe's leading reproductive medicine journal Human Reproduction today.

Principal Investigator at the unit, Professor Richard Sharpe said: "There is now overwhelming evidence that growth and development in foetal life play a fundamental role in determining the future risk of a wide range of common diseases in later life. Male reproductive disorders fall into this category, in particular testicular germ cell cancer, the commonest cancer of young men in their 20s and 30s. We know it originates because of abnormal foetal germ cell development and this then leads to tumour formation in young adulthood, but how and why things go wrong with development of some of the germ cells in foetal life is unknown - and inaccessible for direct study for obvious reasons."

The types of TGCC that occur in humans do not occur in laboratory animals, probably because of differences between humans and animals in the timing and organisation of foetal germ cell development. Therefore, using animal models to study TGCC origins is not possible.

For this reason and because there was no other option available, the researchers obtained ethical approval to take testicular tissue from foetuses that had been aborted at nine weeks and between 14-18 weeks gestation. The women gave consent in accordance with national guidelines. None of the terminations were related to foetal abnormalities.

Testicular tissue cannot be studied in a test tube because it does not survive and develop normally. So the researchers grafted the tissue under the skin of a naturally occurring strain of mice that do not reject tissue grafts because their immune systems do not work normally.

"We found that the testicular graft grows and develops normally over a six-week period; in particular, the foetal germ cells develop normally," said Prof Sharpe. "This means that we have developed a viable system in which we can now test what factors might interfere with this normal germ cell development and push it down the cancer path. For example, we are investigating if exposure to common environmental chemicals, to which human foetuses are exposed in the womb, can cause any such changes in the foetal testis grafts by treating the mouse hosts with these chemicals, an aspect that simply cannot be studied otherwise."

The mouse model may also enable the researchers to study disorders of sexual development (DSDs) in humans, which occur because of abnormal testis development. "DSDs can result from genetic abnormalities involving the sex chromosomes or genes involved in the development of the testes and several of these disorders, such as Frasier or Denys-Drash syndrome, are also associated with a high risk of TGCC," said Prof Sharpe. "In the future, it should be possible to modify

our mouse model so that we can introduce genes that either promote or disrupt normal testicular development and so provide a living model of these conditions. This, in turn, should help us to develop treatments or early interventions for these disorders."

**More information:** Xenografting of human fetal testis tissue: a new approach to study fetal testis development and germ cell differentiation. Human Reproduction journal. doi:10.1093/humrep/deq183

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