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Researchers discover gene required to maintain male sex throughout life

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University of Minnesota Medical School and College of Biological Sciences researchers have made a key discovery showing that male sex must be maintained throughout life.

The research team, led by Drs. David Zarkower and Vivian Bardwell of the U of M Department of Genetics, Cell Biology and Development, found that removing an important male development gene, called Dmrt1, causes male cells in mouse testis to become female cells.

The findings are published online today in *Nature*.

In mammals, sex chromosomes (XX in female, XY in male) determine the future sex of the animal during embryonic development by establishing whether the gonads will become testes or ovaries.

"Scientists have long assumed that once the sex determination decision is made in the embryo, it's final," Zarkower said. "We have now discovered that when Dmrt1 is lost in mouse testes – even in adults – many male cells become female cells and the testes show signs of becoming more like ovaries."

Previous research has shown that removing a gene, called Foxl2, in ovaries caused female cells to become male cells and the ovaries to become more like testes. According to Zarkower, the latest U of M research determines that the gonads of both sexes must actively maintain the original sex determination decision throughout the remainder of life.

For the genetic research community this new understanding is a breakthrough. The findings provide new insight into how to turn one cell type into another, a process known as reprogramming, and also show that throughout life, cells in the testis must be actively prevented from transforming into female cells normally found in the ovary.

"This work shows that sex determination in mammals can be surprisingly prone to change, and must be actively maintained throughout an organism's lifetime," said Dr. Susan Haynes, who oversees developmental biology grants at the National Institute of General Medical Sciences of the National Institutes of Health. "These new insights have important implications for our understanding of how to reprogram cells to take on different identities, and may shed light on the origin of some human sex reversal disorders."

The new findings may force the scientific community to reconsider how disorders involving human sex-reversal occur. Some of these disorders may not result from errors in the original sex determination decision in the embryo, but instead may result from failure to maintain that decision later in embryonic development. In addition, because DMRT1 has been associated with human gonadal cancers, the researchers hope their findings will provide another clue into how gonadal cancer develops.

Provided by University of Minnesota