

Girl with Y chromosome sheds light on maleness

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A seven-year-old girl with a Y chromosome is providing new clues about a possible “master switch” of maleness.

The girl has the normal chromosome count – 46 – and should be male. Other children who have the male sex chromosome but do not appear to be boys have been found to have gene mutations that temper the Y chromosome’s effects. However this child doesn’t have ambiguous gonads, shrivelled testes or other developmental defects. She instead has a normal vagina, cervix and set of ovaries.

A team led by Anna Biason-Lauber, of University Children’s Hospital in Zurich, Switzerland, thinks the patient’s normalcy is due to mutations in a poorly understood gene on chromosome 17 called *CBX2*.

The child’s unique condition might not have been discovered were it not for tests performed before birth to check for major genetic defects, such as an extra copy of chromosome 21 that causes Down’s syndrome. Those tests came up negative and indicated the child would be a boy.

Gene shut-down

When a girl with normal sex organs was born, doctors started scratching their heads. Most females with a Y chromosome have underdeveloped gonads that are prone to developing tumours and usually removed. However, when surgeons operated with the intention of removing the gonads they found normal-looking ovaries in the girl, and took only a tissue sample. This sample, too, looked normal.

Experiments in human cells suggest that the mutations in *CBX2* shut off a gene critical for male sexual development, called *SRY*.

Previous research has shown that mice lacking *CBX2* are sterile, but Biason-Lauber says it’s too early to tell whether her team’s patient will be infertile as well.

“It is quite possible that the ovaries won’t function well,” says John Achermann, a paediatric endocrinologist at University College London’s Institute of Child Health.

“*CBX2* is a predictable and genuine part of the jigsaw puzzle of early human sex development,” Achermann adds. “This gene has been on the agenda for human sex development, but it’s quite important that a case has now been reported.”

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