

A guardian gene for female sex

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Hornless goats.

Researchers at INRA, France, have just uncovered one of the major genes responsible for female differentiation: *FOXL2*. During normal development, the formation of testes or ovaries in a foetus depends on the presence or absence of the *SRY* gene, carried by the Y chromosome. However, instances of sex reversal have been observed, where foetuses carrying two X chromosomes, which are programmed to develop an

ovary, are actually born with all of the characteristics of a male. For more than a decade, researchers at INRA's Developmental Biology and Reproduction unit in Jouy-en-Josas have been studying and characterising the mutations responsible for XX males in domesticated animal species such as goats, exposing the importance of a gene (*FOXL2*) carried by an autosome (not a sex chromosome).

To demonstrate this gene's role in determining gender, the researchers successfully silenced the *FOXL2* gene in goat embryos using new genetic modification techniques. The XX foetuses that no longer had the *FOXL2* gene developed testes instead of ovaries.

Ovaries: to exist, a double front to fight

The female [development](#) process was long considered the "default" [differentiation](#) process. The experiments carried out by the INRA team prove the opposite: that for ovaries to form, feminine [genes](#) must be activated and an active process of silencing must take place to override male development. The *FOXL2* gene acts as a defender of the ovary; as the essential female gene, it silences male genes from the moment the ovary begins to form and a priori throughout development and until adulthood.

A model for studying for female fertility

The *FOXL2* gene was already thought to play an important role in ovarian function in women. The inactivation of one of the two copies of this gene (heterozygous mutation) can in fact cause premature menopause in young women. Thanks to the techniques elaborated by the Developmental Biology and Reproduction unit, a goat model is currently being created to develop innovative therapies (gene or cell) to treat certain causes of female infertility.

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