Alterations in germ cell memory and mini-puberty induce infertility in cryptorchidism

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Background
Spermatogonia harbour P-element induced wimpy testis (Piwi) proteins that associate specifically with Piwi-interactig RNAs (piRNAs) to silence transposable DNA elements. In mice loss-of-function mutations in the Piwi/piRNA pathway lead to de-repression of transposable elements, resulting in germ cell death and sterility.

Patients and methods
Microarray analysis included 19 testicular biopsies from cryptorchid patients, classified into: high infertility risk group (HIR, n = 7), which lacked Ad spermatogonia due to impaired mini-puberty, and low infertility risk group (LIR = 12), which completed transformation from gonocytes into Ad spermatogonia during mini-puberty. EPON-embedded biopsies were analyzed by TEM.

Results and discussion

Impaired mini-puberty:

↓DDX4/DDX25
↓Piwi/piRNA pathway

↓EGR4

Altered P- bodies **

↓MORC1

Transposon de-repression

Germ cell apoptosis

INFERTILITY


Conclusion
Cryptorchidism-induced infertility is associated with alterations in the Piwi/piRNA-pathway and other transposon-silencing genes such as MORC1. Intact mini-puberty appears to be essential for the development of the endogenous defense system against transposable elements and establishment of germ cell memory. At the level of spermatogonia, temperature appears to have only a negligible effect.