The endometrium of women with endometriosis and other implantation disorders shows reduced expression of HOXA10. This defect may underlie the decreased receptivity of the endometrium to embryo implantation that often afflicts women with endometriosis.

Sex steroid levels are not affected in women with endometriosis and so do not account for decreased HOXA10 expression; Raefella Petracco et al. searched for an alternative culprit. They employed bioinformatics software to predict which microRNAs might regulate the HOXA10 gene and landed on MIR135A and MIR135B.

The researchers found that both microRNAs are expressed in a pattern that suggests a role in HOXA10 regulation. They are both expressed in the endometrium of healthy women and MIR135A is expressed cyclically, peaking when HOXA10 levels are lowest. Expression of both microRNAs is elevated in women with endometriosis, most dramatically during the proliferative phase of the cycle, when HOXA10 expression is low.

These correlative studies were supported by transfection experiments using endometrial cells, which showed that the two microRNAs regulate HOXA10. The microRNAs reduced expression of a luciferase gene hooked to the HOXA10 3’ UTR in endometrial stromal cells, but did not reduce reporter expression in an unrelated cell type, MCF-7 cells. The data suggest that MIR135A and MIR135B operate in context with other factors found specifically in endometrial cells.

The findings reveal a new potential therapeutic target for endometriosis, a difficult-to-treat and poorly understood condition.


Depleting DICER1 Mauls Male Germ Cells
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The enzyme DICER1 is essential for the biogenesis of several small classes of RNAs, including microRNAs (miRNAs) and endogenous small interfering RNAs (endo-siRNAs), both of which have been implicated in numerous biological processes. Dicer 1 is also essential for degrading toxic transposable elements.

Previously, two groups of researchers had knocked out DICER1 in the male germline using Cre recombinase–expressing mice. The mice had had impaired fertility due to defects such as poor sperm motility. But the authors of the new study, Yannick Romero et al., say that DICER1 may not have been completely knocked out in these studies—for instance, Cre was hooked up to a promoter that drove its expression in only about half of all male germ cells. Romero et al. knocked DICER1 out cold by driving Cre with a different promoter, that for the germline factor DDX4 (also known as Vasa).

The researchers found that DICER1 was not required for spermatogonial stem cell renewal and mitotic proliferation, but the enzyme was required for meiosis, with defects emerging prior to prophase I and the haploid stage of spermatogenesis. Alterations included delayed progression of meiotic prophase I and an increase in apoptosis in spermatocytes. The few spermatids found in the mice had various defects, such as abnormal head shape and immotility. Dicer1-