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Oocyte-specific gene mutations cause premature ovarian failure

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Mutations in a gene called FIGLA cause premature ovarian failure in at least a percentage of women who suffer from the disorder, said researchers from Baylor College of Medicine in Houston and Shandong University in China in a report that appears online today in the *American Journal of Human Genetics*.

“We hope to use the information from this study and others that identify genes associated with this problem to find biomarkers in blood that can help us determine a woman’s risk of early infertility,” said Dr. Aleksandar Rajkovic, associate professor of obstetrics and gynecology at BCM and senior author of the paper. Premature ovarian failure, which means that the ovaries lose function before age 40, not only causes infertility but also bone and heart problems, he said.

“It affects 1 percent of women,” he said. “While most people associate it with infertility, women with premature ovarian failure face an increased risk of cardiovascular disease, osteoporosis and premature death. Ovarian reserves are important for women’s health.”

In looking for genes that cause the disorder, Rajkovic and his colleagues here and in China concentrated on those that are most likely to function in the ovary. A gene mutation does not totally halt gene activity, but Rajkovic believes it can accelerate the loss of eggs (or germ cells). When all the eggs are lost, the ovaries stop producing estrogen, leading to menopause symptoms.

In this study, Rajkovic and his collaborators screened 100 Chinese women with premature ovarian failure for mutations in FIGLA and found three different kinds of mutations in the FIGLA genes of four.

FIGLA is one of four transcription factors found to control the differentiation of egg cells early in development. Transcription factors govern the activity of genes, turning them off and on and modulating the extent to which they are active.

The other genes involved include NOBOX, GDF9 and BMP 15, said Rajkovic. Mutations in these can lead to premature ovarian failure as well, he said.

“We hope to define majority of the genes that are part of the cellular pathways involved in ovarian failure,” said Rajkovic. “Ideally in the future we will offer a test to women to look at all the genes involved in premature ovarian failure.”

He anticipates that a gene chip would be helpful in such diagnosis, which can help in counseling women or their children about the risk of early ovarian failure.

Source: Baylor College of Medicine