REPRODUCTIVE ENDOCRINOLOGY

EPIGENETICS IN PREGNANCY

New research suggests that mammary glands retain an 'epigenetic memory' of pregnancy that changes the response to subsequent pregnancies.

Previous evidence indicates that the response to a second pregnancy is different to the response to a first pregnancy. For example, milk supply is often increased after a second pregnancy compared with after a first pregnancy. Now, Camila dos Santos and colleagues hypothesize that these changes are accomplished via long-lasting modifications to the epigenome.

The investigators started by assessing the response to first and subsequent pregnancies in mice. Nulliparous and uniparous mice were implanted with slow-release estrogen/progesterone pellets that mimicked the effects of pregnancy. Mammary glands were harvested at 6 days and 12 days after implantation. The uniparous mice responded to the pregnancy hormones earlier and had a greater number of ductal structures than the nulliparous mice. Milk production was also initiated earlier in the uniparous mice than in the nulliparous mice.

dos Santos and co-workers then analysed the epigenetic characteristics of the two groups of mice. "We found that pregnancy induces substantial loss of DNA methylation in mammary epithelial cells," explains dos Santos. "These changes were concentrated at genes with a role in cell proliferation and lactation, two major biological processes activated during pregnancy." The epigenetic changes were largely located at sites occupied by Stat5a, a transcription factor that regulates pregnancy-induced development of the mammary glands. The team also demonstrated that the loss of DNA methylation induced by the first pregnancy led to rapid reactivation of the affected genes in a subsequent pregnancy. "This association is probably one of the main components of the mammary gland differential reaction to a second pregnancy," says dos Santos.

Pregnancy is known to affect the risk of breast cancer. As such, dos Santos and colleagues are now planning to investigate whether the effects of pregnancy on the epigenome of mammary glands is involved in the protective effect of early pregnancy on risk of breast cancer.

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