

Maternal diabetes impairs methylation of imprinted gene in oocytes

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For the first time, researchers have shown that poorly controlled maternal diabetes has an adverse effect on methylation of the maternal imprinting gene *Peg3*, contributing to impaired development in offspring.

Previous studies have revealed that offspring of diabetic mothers display a higher incidence of malformations and fetal death, even when a one-cell embryo is transplanted from a diabetic to a non-diabetic mother. Diabetic mothers' oocytes tend to exhibit reduced [glucose metabolism](#), compromised communication between [cumulus cells](#) and oocytes, mitochondrial malfunction, and a decreased ovulation rate, all of which can be traced back to reduced gene expression in the embryos.

Qing-Yuan Sun and Zhao-Jia Ge of the [Chinese Academy of Sciences](#) hypothesized that the reduced gene expression results from disturbed DNA re-methylation during oogenesis and oocyte maturation. The team bred and examined three different mouse populations: one with spontaneously occurring diabetes, one with diabetes induced by STZ injection, and one without diabetes. After mating on Day 15, the diabetic mice presented with reduced [pregnancy rates](#) (approx. 74% vs. 100% in non-diabetic mice) and increased embryo death rates (approx. 16% vs. 0%), consistent with previous reports.

Focusing on the methylation patterns of one paternally methylated gene (*H19*) and two maternally methylated genes (*Peg3* and *Snrpn*), the team found that none showed impaired methylation until 35 days after STZ

injection; however, [embryo development](#) and number of offspring were already affected on Day 15. On Day 35, methylation of *Peg3* was significantly decreased, with an unmethylated oocyte rate nearly 22% higher in both types of [diabetic mice](#) compared to controls. *H19* remained unaffected and effects on *Snrpn* were not significant.

As for the female offspring of diabetic mothers, their oocytes did not appear to have any methylation abnormalities; however, due to the difficulty of producing offspring conceived after Day 15, it will be extremely difficult to determine whether those females are similarly unaffected.

More information: Ge ZJ, Liang XW, Guo L, Liang QX, Luo SM, Wang YP, Wei YC, Han ZM, Schatten H, Suna QY. Maternal diabetes causes alterations of DNA methylation statuses of some imprinted genes in murine oocytes. *Biol Reprod* 2013; (in press). Published online ahead of print, March 2013; [DOI 10.1095/biolreprod.112.105981](https://doi.org/10.1095/biolreprod.112.105981)

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