

## Alteration in expression and methylation of IGF2/H19 in placenta and umbilical cord blood are associated with macrosomia exposed to intrauterine hyperglycemia

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**Objective:** Macrosomia is one of the most common complications in gestational diabetes mellitus. Insulin-like growth factor 2 and H19 are two of the imprinted candidate genes that are involved in fetal growth and development. Change in methylation at differentially methylated region of the insulin-like growth factor 2 and H19 has been proved to be an early event related to the programming of metabolic profile, including macrosomia and small for gestational age in offspring. Here we hypothesize that alteration in methylation at differentially methylated region of the insulin-like growth factor 2 and H19 is associated with macrosomia induced by intrauterine hyperglycemia. **Results:** The expression of insulin-like growth factor 2 is significant higher in gestational diabetes mellitus group (GDM group) compared to normal glucose tolerance group (NGT group) both in umbilical cord blood and placenta, while the expression of H19 is significant lower in GDM group in umbilical cord blood. The expression of insulin-like growth factor 2 is significant higher in normal glucose tolerance with macrosomia group (NGT-M) compared to normal glucose tolerance with normal birthweight group (NGT-NBW group) both in placenta and umbilical cord blood. The methylation level at different CpG sites of insulin-like growth factor 2 and H19 in umbilical cord blood was also significantly different among groups. Based on the multivariable linear regression analysis, the methylation of the insulin-like growth factor 2 / H19 is closely related to birth weight and intrauterine hyperglycemia. **Conclusions:** We confirmed the existence of alteration in DNA methylation in umbilical cord blood exposed to intrauterine hyperglycemia and reported a functional role in regulating gene associated with insulin-like growth factor 2/H19. Both of these might be the underlying pathogenesis of macrosomia. We also provided the evidence of strong associations between methylation of insulin-like growth factor 2/H19 and macrosomia induced by intrauterine hyperglycemia.