Obesity and diabetes in pregnancy: Consequences in offspring

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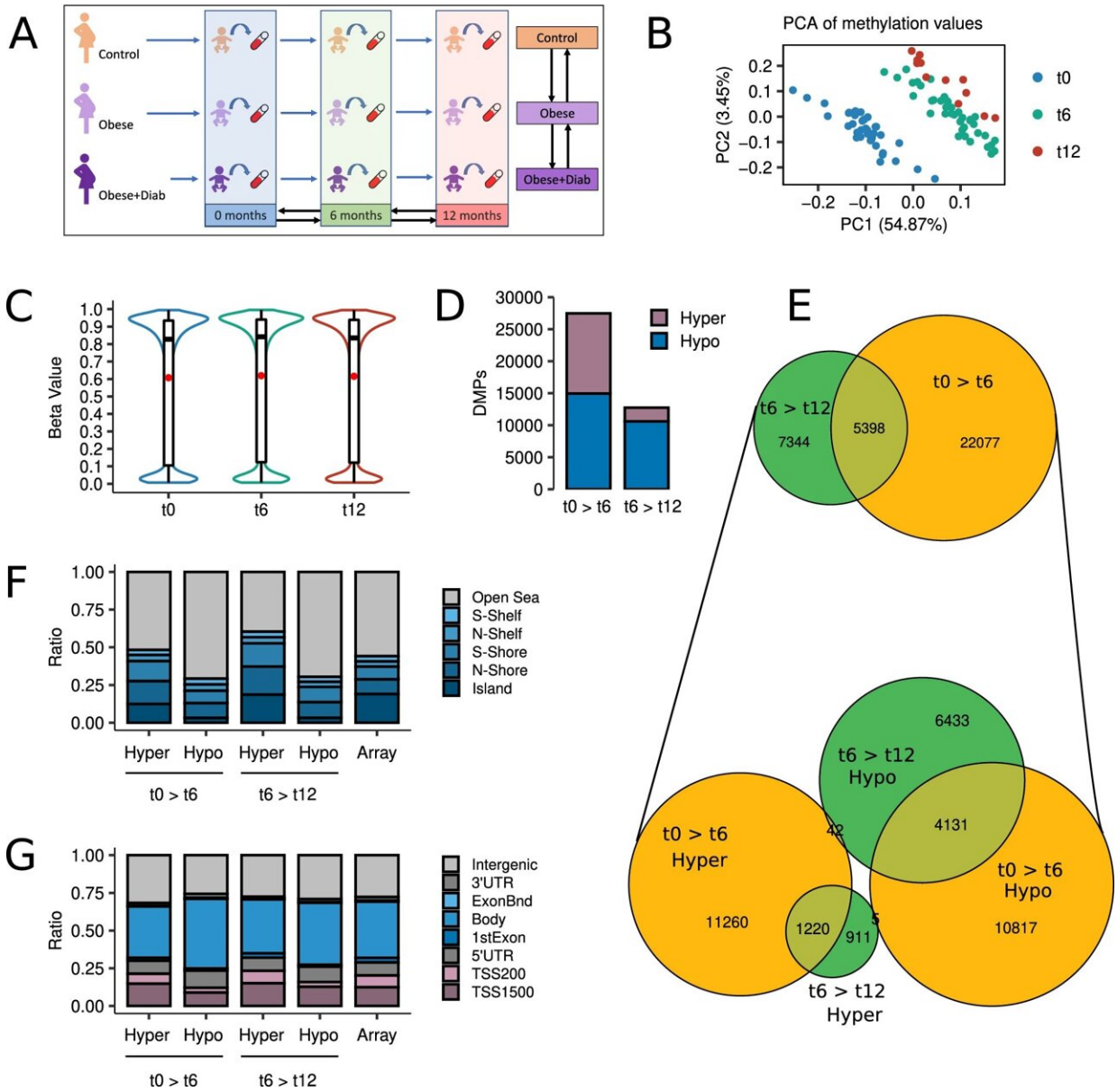

Development is the main origin of methylation changes during the first year of life. **a** Schematic of the study design. **b** Scatter plot showing the PCA of the subjects according to their methylation values at the top 100,000 most variable CpG sites. **c** Violin plots describing the distribution of methylation values at the 772,088 CpGs analyzed by time point. **d** Barplots depicting the number of hyper- and hypomethylated DMPs (FDR 6 and 6 > 12 longitudinal comparisons. **e** At the top, a Venn diagram showing the intersections between 0 > 6 and 6 > 12 DMPs. At the bottom, a Venn diagram describing the intersection between hyper- and hypomethylated DMPs at 0 > 6 and 6 > 12 comparisons. **f** Barplots showing the relative distribution of hyper- and hypomethylated DMPs at 0 > 6 and 6 > 12 comparisons according to their CpG island location status. **g** Barplots showing the relative distribution of hyper- and hypomethylated DMPs at 0 > 6 and 6 > 12 comparisons according to their gene location status. Rightmost bars represent the background distribution considering all 772,088 probes analyzed. Credit: *Cardiovascular Diabetology* (2023). DOI: 10.1186/s12933-023-01774-y

Research involving pediatricians from the Hospital General de Valencia has shown that the children of women who were obese or had diabetes during pregnancy developed certain epigenetic alterations that predisposed them to suffer from diseases such as diabetes, obesity and the cardiovascular problems that result from them. This risk not only exists during childhood and adolescence, but is also maintained in later stages of life.

The study, published in *Cardiovascular Diabetology*, was carried out by pediatricians from the Hospital General de Valencia, which belongs to the Centro de Investigación Biomédica en Red (CIBER) on Physiopathology of Obesity and Nutrition (CIBEROBN), the University of Valencia and the INCLIVA Health Research Institute of Valencia, in collaboration with scientists from the Epigenetics and Nanomedicine research group (CINN-CSIC), the University of Oviedo, and the CIBER on Rare Diseases (CIBERER).

According to Empar Lurbe, Principal Investigator of the CIBEROBN Group, "Pregnancy is a fundamental period in the life of human beings that actively affects the development of offspring and their predisposition to the future appearance of cardiometabolic diseases. Disorders such as maternal obesity and gestational diabetes can condition the health of the offspring, from infancy to adulthood, increasing the risk of comorbidities that reduce quality of life and life expectancy."

On the other hand, and in the opinion of Mario Fraga of CIBERER, another of the coordinators of the study, "Maternal obesity during pregnancy can affect up to 30% of pregnant women, with the resulting repercussions for health systems and their public health policies. However, beyond the epidemiological evidence, the molecular causes responsible for these negative effects on the health of the offspring are unknown."

The study describes epigenetic alterations in the offspring, beyond birth, associated with the maternal metabolic condition during gestation. These chemical modifications influence gene regulation, and their alteration is behind the development of multiple diseases of great social impact, such as obesity.

To reach these conclusions, an analysis was performed in a pediatric cohort of children born to mothers with obesity or obesity with gestational diabetes. One of the greatest strengths of the study is the longitudinal follow-up, which has been carried out throughout the first year of life in the Pediatrics Department of the Hospital General de Valencia, and which has made it possible to clarify the molecular traces by which mothers are able to influence the genome of their offspring continuously over time.

The researchers explain how this study represents a new example of how the environment interacts with our genes. In this case, the results indicate

that the health status and metabolic condition of the pregnant mother can persistently condition the health status of the offspring, which may have important implications for public health issues.

This work constitutes the first evidence that the intrauterine environment and, more specifically, obesity and gestational diabetes, are capable of persistently reprogramming the methylation patterns of offspring beyond birth.

The alterations involve genes that are part of regulatory pathways of fatty acid metabolism, cardiovascular signaling or mitochondrial bioenergetics, crucial processes in obesity and diabetes mellitus. Being able to detect these alterations in peripheral blood reinforces the idea that maternal metabolism has systemic effects on child development.

More information: Juan José Alba-Linares et al, Maternal obesity and gestational diabetes reprogram the methylome of offspring beyond birth by inducing epigenetic signatures in metabolic and developmental pathways, *Cardiovascular Diabetology* (2023). DOI: 10.1186/s12933-023-01774-y

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