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Differences between human twins at birth highlight importance of intrauterine environment

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Your genes determine much about you, but environment can have a strong influence on your genes even before birth, with consequences that can last a lifetime. In a study published online in *Genome Research*, researchers have for the first time shown that the environment experienced in the womb defines the newborn epigenetic profile, the chemical modifications to DNA we are born with, that could have implications for disease risk later in life.

Epigenetic tagging of genes by a chemical modification called DNA methylation is known to affect gene activity, playing a role in normal development, aging, and also in diseases such as diabetes, heart disease, and cancer. Studies conducted in animals have shown that the environment shapes the epigenetic profile across the genome, called the epigenome, particularly in the womb. An understanding of how the intrauterine environment molds the human epigenome could provide critical information about disease risk to help manage health throughout life.

Twin pairs, both monozygotic (identical) and dizygotic (fraternal), are ideal for epigenetic study because they share the same mother but have their own umbilical cord and amniotic sac, and in the case of identical twins, also share the same genetic make-up. Previous studies have shown that methylation can vary significantly at a single gene across multiple tissues of identical twins, but it is important to know what the DNA

methylation landscape looks like across the genome.

In this report, an international team of researchers has for the first time analyzed genome-scale DNA methylation profiles of umbilical cord tissue, cord blood, and placenta of newborn identical and fraternal twin pairs to estimate how genes, the shared environment that their mother provides and the potentially different intrauterine environments experienced by each twin contribute to the epigenome. The group found that even in identical twins, there are widespread differences in the epigenetic profile of twins at birth.

"This must be due to events that happened to one twin and not the other," said Dr. Jeffrey Craig of the Murdoch Childrens Research Institute (MCRI) in Australia and a senior author of the report. Craig added that although twins share a womb, the influence of specific tissues like the placenta and umbilical cord can be different for each fetus, and likely affects the epigenetic profile.

Interestingly, the team found that methylated genes closely associated with birth weight in their cohort are genes known to play roles in growth, metabolism, and cardiovascular disease, lending further support to a known link between low birth weight and risk for diseases such as diabetes and heart disease. The authors explained that their findings suggest the unique environmental experiences in the womb may have a more profound effect on epigenetic factors that influence health throughout life than previously thought.

Furthermore, an understanding of the epigenetic profile at birth could be a particularly powerful tool for managing future health. "This has potential to identify and track disease risk early in life, said Dr. Richard Saffery of the MCRI and a co-senior author of the study, "or even to modify risk through specific environmental or dietary interventions."

More information: Gordon L, Joo JE, Powell JE, Ollikainen M, Novakovic B, Li X, Andronikos R, Cruickshank MN, Conneely KN, Smith AK, Alisch RS, Morley R, Visscher PM, Craig JM, Saffery R. Neonatal DNA methylation profile in human twins is specified by a complex interplay between intrauterine environmental and genetic factors, subject to tissue-specific influence. *Genome Res* doi: 10.1101/gr.136598.111