Risk of obesity influenced by changes in our genes

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This is an image of a weight scale. Credit: CDC/Debora Cartagena

These changes, known as epigenetic modifications, control the activity of our genes without changing the actual DNA sequence. One of the main epigenetic modifications is DNA methylation, which plays a key role in embryonic development and the formation of different cell types, regulating when and where genes are switched on.

Although DNA methylation was originally thought to be a very stable modification, which once established in early life was then maintained throughout the life span of an individual, there is now growing evidence that the level of DNA methylation can be affected by a range of environmental factors such as parental health, diet and lifestyle.

Researchers from the University of Southampton, as part of the EpiGen Global Consortium, analysed the levels of DNA methylation, in umbilical cord tissue of babies born in the Southampton Women's Survey.

They compared DNA methylation levels present at birth with the amount of fat tissue in the child at four and six years of age. They found that lower DNA methylation at the CDKN2A gene, which regulates the production of fat cells, was associated with a greater risk of the child developing obesity in later life.

Analysis showed that a 10 percent decrease in methylation at the CDKN2A gene was associated with an increase in fat mass of around 220g, at age 4 years.

The results, published in *EBio Medicine*, were replicated in other groups of children and adults, notably the Singapore GUSTO study, the Australian RAINE study and the UK BIOCLAIMS cohort.

Lead author Karen Lillycrop said: "This is exciting new evidence that epigenetic changes detectable at birth are linked to a child's health as they grow up. It was very promising to see our initial findings confirmed in so many other cohorts. Not only does it strengthen the body of evidence that shows a mothers health during pregnancy can affect the future health of her child, but it could also allow us to more accurately predict the future risk of obesity. If we can do this, then preventative strategies can be developed in early life to prevent the development of

obesity."

Professor Keith Godfrey, from the Medical Research Council Lifecourse Epidemiology Unit and the National Institute for Health Research Southampton Biomedical Research Centre and a member of the study team said: "The new findings provide the first direct evidence linking faltering of a baby's growth in the womb with epigenetic modifications that themselves may increase the risk of childhood obesity. The findings are now helping us to trial new nutritional interventions before and during pregnancy to reduce the baby's risk on obesity in childhood and later life, and strengthen the view that effective prevention of childhood obesity has to begin before the baby is born. The new findings may also lead to innovative approaches to the treatment of established obesity in later life."

More information: ANRIL promoter DNA methylation: a perinatal marker for later adiposity, *EBio Medicine*, 2017.

Provided by University of Southampton