Medical Xpress

Mother's diet in pregnancy may have lasting effects for offspring

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A poor diet during pregnancy can cause biological changes that last throughout life, according to research from Imperial College London.

The study, published this week in the journal *Cell Reports*, showed that when pregnant mice were fed a diet deficient in protein this interfered with the expression of genes within the embryo that are known to be important for healthy growth.

The impact of adversity, such as a poor diet in early life, and whether this might cause lasting effects has long intrigued scientists. There have been suggestions that the children of women pregnant during famines, for example, may suffer harmful effects later in life. This new study offers a new way to visualise such effects and possible ways to counter these.

The researchers, at the Medical Research Council London Institute of Medical Sciences (MRC LMS), developed novel imaging techniques that enabled them to visualise genes as they were switched "on" or "off" in mouse embryos as they grew. This enabled the team to see exactly where alterations in response to maternal diet were happening and, crucially when during pregnancy key changes took place.

Understanding how genes are controlled and kept "on" or "off" is a relatively new field of science known as "epigenetics". This is the first time such epigenetic effects have been visualised during development in this way, using a simple but powerful bioluminescent imaging approach.

The team attached enzymes from fireflies (luciferase) or bacteria (beta-galactosidase) onto the gene they were studying, and watched how this produced a glow as the gene was turned "on" in mice.

The research focused on a group of genes called "imprinted" genes, and on one in particular known as Cdkn1c. Imprinted genes are intriguing because although a copy of the gene is inherited from each parent, as usual, only one of these copies is active. The other copy is kept idle, or "silenced". In the case of Cdkn1c, only the copy inherited from the mother is active.

Using their new visualising technique, the team showed that if a mouse carried the copy of the gene from the father, which is "silenced", then it could not be seen. If they used either diet or drugs to re-activate it, they were able to see the gene glow. The researchers expect that this new way to "see" when imprinted genes are active or silent will prove valuable for many other scientists who are investigating epigenetic effects in our bodies.

Imprinted genes

"There are around 100 imprinted genes, about 0.4% of the total in the genome, and most appear to have their greatest impact during pregnancy. The pattern by which imprinted genes are 'set' in early life plays an important part in the development of healthy offspring. If a gene is 'miss-set' then problems may occur later," says Dr Mathew Van de Pette, a lead author based at the MRC LMS.

He added: "We found that mice fed a low protein diet in pregnancy produced offspring in which the father's copy of the gene became active and stayed that way. This demonstrates a clear link between early life adversity and later life outcomes."

"We were surprised that this change in diet permanently affected the expression of this imprinted gene," said Professor Amanda Fisher, who led the study and is director of the MRC LMS. "Our work suggests there may be a window of vulnerability when diet can indeed have an effect, and that once these genes are set, they're set for life," Professor Fisher said. "The good news is that we've also shown that it's possible to avoid this with a normal diet."

More information: Mathew Van de Pette et al. Visualizing Changes in

Cdkn1c Expression Links Early-Life Adversity to Imprint Mis-regulation in Adults, *Cell Reports* (2017). DOI: 10.1016/j.celrep.2017.01.010

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