Mother's diet affects the 'silencing' of her child's genes

April 29 2014

Images of research from the Gambia are shown here. Credit: Felicia Webb

A mother's diet before conception can permanently affect how her child's genes function, according to a study published in *Nature Communications*.

The first such evidence of the effect in humans opens up the possibility that a mother's diet before pregnancy could permanently affect many aspects of her children's lifelong health.

Researchers from the MRC International Nutrition Group, based at the London School of Hygiene & Tropical Medicine and MRC Unit, The Gambia, utilised a unique 'experiment of nature' in rural Gambia, where the population's dependence on own grown foods and a markedly seasonal climate impose a large difference in people's dietary patterns between rainy and dry seasons.

Through a selection process involving over 2,000 women, the researchers enrolled pregnant women who conceived at the peak of the rainy season (84 women) and the peak of the dry season (83 women). By measuring the concentrations of nutrients in their blood, and later analysing blood and hair follicle samples from their 2-8 month old infants, they found that a mother's diet before conception had a significant effect on the properties of her child's DNA.

While a child's genes are inherited directly from their parents, how these genes are expressed is controlled through 'epigenetic' modifications to the DNA. One such modification involves tagging gene regions with chemical compounds called methyl groups and results in silencing the genes. The addition of these compounds requires key nutrients including folate, vitamins B2, B6 and B12, choline and methionine.

Images of research in the Gambia are shown here. Credit: Felicia Webb

Experiments in animals have already shown that environmental influences before conception can lead to epigenetic changes that affect the offspring. A 2003 study found that a female mouse's diet can change her offspring's coat colour by permanently modifying DNA methylation.1 But until this latest research, funded by the Wellcome Trust and the MRC, it was unknown whether such effects also occur in humans.

Senior author Dr Branwen Hennig, Senior Investigator Scientist at the MRC Gambia Unit and the London School of Hygiene & Tropical Medicine, said: "Our results represent the first demonstration in humans that a mother's nutritional well-being at the time of conception can change how her child's genes will be interpreted, with a life-long impact."

The researchers found that infants from rainy season conceptions had consistently higher rates of methyl groups present in all six genes they studied, and that these were linked to various nutrient levels in the mother's blood. Strong associations were found with two compounds in particular (homocysteine and cysteine), and the mothers' body mass index (BMI) had an additional influence. However, although these epigenetic effects were observed, their functional consequences remain unknown.

Images of research in the Gambia are shown here. Credit: Felicia Webb

Professor Andrew Prentice, Professor of International Nutrition at the London School of Hygiene & Tropical Medicine, and head of the Nutrition Theme at the MRC Unit, The Gambia, said: "Our on-going research is yielding strong indications that the methylation machinery can be disrupted by nutrient deficiencies and that this can lead to disease. Our ultimate goal is to define an optimal diet for mothers-to-be that would prevent defects in the methylation process. Pre-conceptional folic acid is already used to prevent defects in embryos. Now our research is pointing towards the need for a cocktail of nutrients, which could come from the diet or from supplements."

Dr Rob Waterland of Baylor College of Medicine in Houston, who conducted the epigenetic analyses said: "We selected these gene regions because our earlier studies in mice had shown that establishment of DNA methylation at metastable epialleles is particularly sensitive to maternal nutrition in early pregnancy."

The authors note that their study was limited by including only one blood sampling point during early pregnancy, but estimates of pre-conception nutrient concentrations were calculated using results from non-pregnant women sampled throughout a whole calendar year. The authors also plan to increase the sample size in further studies.

More information: Maternal nutrition at conception modulates DNA methylation of human metastable epialleles. Paula Dominguez-Salas, Sophie E. Moore, Maria S. Baker, Andrew W. Bergen, Sharon E. Cox, Roger A. Dyer, Anthony J. Fulford, Yongtao Guan, Eleonora Laritsky, Matt Silver, Gary E. Swan, Steven H. Zeisel, Sheila M. Innis, Robert A. Waterland, Andrew M. Prentice & Branwen J. Hennig. *Nature Communications*. DOI: 10.1038/ncomms4746

Provided by London School of Hygiene & Tropical Medicine